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ANAPHYLACTOGENIC PROPERTIES OF CERTAIN CEREAL FOODS AND BREADSTUFFS

ALLERGENIC DENATURATION BY HEAT

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Although there may be a vast amount of disagreement with respect to the underlying mechanism of allergy and the diagnostic procedures to be employed, it is generally agreed that the method of choice in the first stage of treatment of food allergy is the exclusion of the offending food from the patient's diet. If the patient is sensitive to a single food, the problem is comparatively simple. Multiple sensitivity presents a more difficult situation. It is obvious that wholesale elimination of various genera of food substances may give rise to nutritional and psychogenic disturbances, particularly in infancy and in childhood. Substitution has been tried as an alternative measure with only fair success, perhaps mainly for the reason that the chief offenders are milk, wheat and egg, for which adequate substitutes are not readily found. The problem, therefore, is to find a better way to cope with the situation.

The fact that heat diminishes the antigenicity of proteins is known. The alteration is largely dependent on physicochemical changes which result from the coagulation and flocculation of the soluble protein fractions. Few studies, however, have thus far been made on the practical application of denaturation by heat to foods in general.

Clinical experience led the pediatrician to the use of evaporated milk for the infant sensitive to milk. Several years ago we sought to investigate experimentally the alteration that enables a patient to tolerate a heated food which in its raw state provokes allergic reactions. Such information could not be arrived at by way of clinical experience with any degree of accuracy or dispatch and without procedures which were prejudicial to health.

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In our studies with milk [1] we utilized the experiment with anaphylaxis in the guinea pig which offers an accurate biologic measure of the relative antigenicity of proteins. The immunologic reactions are of considerably greater delicacy than either the results of the chemical test or clinical observation. Whether results obtained in the lower animal can be applied directly to the human being may be questioned. We believe, however, that the phenomena of anaphylaxis in the animal and allergy in the human being have been sufficiently correlated to make knowledge of the relative antigenicity of the various forms of prepared foods in the lower animal of practical value in the treatment of the human subject.

In the present investigation, certain cooked and commercially prepared cereal foods and breadstuffs were subjected to study in order that their relative anaphylactogenicity might be determined.

EXPERIMENTAL INVESTIGATION

Material.—One of the criteria laid down by Wells [2] for the production of anaphylaxis is that an antigen must be in a soluble state in order to take part in the anaphylactic reaction. In our experiments, therefore, we used the soluble fractions of raw and cooked grain foods which readily enter into solution when subjected to weak alkali. Wells and Osborne [3] used purified proteins in their experiments. For the most part, they were the alcohol-soluble fractions which were dissolved in a 0.2 per cent solution of sodium hydroxide for injection. These investigators were primarily interested in the comparative biologic reactivity of the various protein fractions in vegetables and in other protein food substances. They were therefore compelled to separate and purify such fractions to the highest degree. We were primarily interested in studying the whole grain as it is consumed by the subject. The whole grain substance, which contained all the protein, was therefore used instead of any single element. What fractions went into solutions we are unable to state.

Extracts were made from: (1) raw cereal grains; (2) grain foods which ordinarily require preparation in the home before using and which we shall designate as home-cooked foods; they included boiled cereals, cereal pastes, pancakes, waffles, breads, cakes and puddings; (3) certain precooked foods such as dry cereals, biscuits and crackers.

The dry materials were weighed and mixed with hundredth-normal potassium hydroxide in the proportion of 1 Gm. to 10 cc. of the alkali. All extractions with alkali were made at room temperature in order that denaturation by the alkali might be avoided.

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1. Ratner, B., and Gruehl, H. L.: Anaphylactogenic Properties of Milk; Immunochemistry of Purified Proteins and Antigenic Changes Resulting from Heat and Acidification, Am. J. Dis. Child. **49**:287 (Feb.) 1935.

2. Wells, H. G.: The Present Status of the Problems of Anaphylaxis, Physiol. Rev. **1**:44, 1921.

3. Wells, H. G., and Osborne, T. B.: The Biological Reactions of the Vegetable Proteins, J. Infect. Dis. **8**:66, 1911.

The extracts made from cooked cereals were prepared as follows: The raw materials were weighed and then cooked in boiling water for the required time. After being cooled to room temperature, the alkali was added to the cooked cereal in proportion to the weight of the original dry substance. The mixture was stirred in an electric mixer for one hour. It was then centrifuged and filtered through a Seitz filter for sterilization and for elimination of any particles which might produce anaphylactoid reactions and thus interfere with the proper appraisal of the reaction resulting from intravenous injection.

The speed of filtration varied. Rice and corn were filtered readily; farina and rye, slowly, and barley and oats, with great difficulty. Filtration of the cooked cereals was sluggish, probably because of the large amount of cooked starch present. During stirring, they were broken into fine particles which did not come down entirely on centrifugation, but remained to clog the filter.

Foods were not defatted before extraction, because the alkali saponified the fats, which rose to the top during centrifugation and could be easily removed.

The final extracts were crystal clear and ranged from dark amber to colorless, according to the color of the original substance.

All solutions, whether for sensitization or shock, were freshly made for each day's experiments.

Protein Tests.—The biuret, Millon and Hopkins-Cole tests were made on all extracts when the color of the solution did not interfere.

Anaphylactic Test.—Normal guinea pigs weighing between 250 and 350 Gm. were used for these experiments. They were obtained from a reliable source, and in no instance was any animal used that reacted abnormally to the preliminary sensitizing injection.

The dose was uniform for all animals. Each received 10 cc. intraperitoneally as a sensitizing dose and, three weeks later, 0.5 cc. intravenously as a shock dose.

For the main thesis of this study, the animals were sensitized with the raw materials, and the homologous cooked products were used as shock agents. In order to determine, however, whether any change in specificity resulted from cooking, certain experiments were performed in which the cooked products were used as sensitizing agents.

Every animal received a second dose, the control shock dose, in order that we might determine whether it was sensitized to the original substance; the second injection was given one hour after the first. The question of desensitization might be raised, but it is evident from our protocols (table 6) that no desensitization occurred. Animals gave a positive control shock reaction when they reacted negatively to the control product. A negative reaction with a cooked product might appear to give evidence of a reduction in antigenicity, whereas the animal actually might not have been sensitized to the raw material. We believe this is an important criterion in studies in which various forms of related substances are compared. The control reaction served also as a measure by which the degree of the reduction in anaphylactogenicity of the denatured food could be evaluated.

Influence of Previous Diet on the Anaphylactic Reaction.—A factor that must be considered in studies on anaphylaxis with cereal proteins is the animal's previous diet. Several investigators (Rosenau and Anderson; Wells and Osborne and we,[4] among others) have shown that proteins fed to experimental animals may

4. For bibliography see Ratner, B., and Gruehl, H. L.: Passage of Native Proteins Through the Normal Gastro-Intestinal Wall, J. Clin. Investigation **13**: 517, 1934.

enter the blood stream in a native state in amounts sufficient to produce sensitization. Wells and Osborne, however, found that after prolonged feeding the animals reacted less strongly to these proteins and finally acquired immunity. From this it might be assumed that animals which ordinarily receive oats, corn or other grains in their diet may be sensitized or refractory to these grains.

While they were bred and during their stay in our laboratory our animals had received a diet which consisted largely of fresh green vegetables, oats and a commercial feed.[5]

Data recorded in table 6 suggest that immunity may have been established in some of the animals which failed to become sensitized to oats and other grains. There appeared to be little refractoriness to wheat, rye and rice.

Some animals showed transient irritation after the primary intraperitoneal sensitizing injection, jumping up and down and arching their backs as if to relieve intraperitoneal pressure. The animals appeared to be in distress for one and a half to two minutes, but recovered rapidly. This may be attributed to mild sensitization resulting from their diet, as Wells and Osborne [3] observed in their experiments.

TABLE 1.—*Relative Anaphylactogenicity of the Raw Cereal Extracts* *

Grain	Number of Animals	Relative Reactivity†					Results, Percentages	
		++++	+++	++	+	0	Positive	Negative
Rice	70	15	34	9	4	8	89	11
Wheat	75	27	18	11	9	10	87	13
Rye	70	13	20	14	12	11	85	15
Corn	98	4	15	22	25	32	67	33
Barley	40	0	0	2	8	30	25	75
Oats	46	0	0	0	7	39	15	85

* All animals were sensitized with 10 cc. of an alkaline extract injected intraperitoneally and were shocked three weeks later with 0.5 cc. injected intravenously.

† In these headings ++++ indicates death: +++, convulsions, collapse and recovery; ++, severe dyspnea, convulsions and recovery; +, dyspnea and irritability, and 0, no reaction.

In order to clarify this point further, we injected intravenously into normal animals raw extracts (0.5 cc.) of wheat, rice, oat, corn and rye, using 10 animals for each grain. Since no reactions occurred from the primary intravenous injection, we believe that the irritative peritoneal reaction is not indicative of anything more than mild hypersensitivity, which is of no significance for a proper evaluation of our experiments.

RAW GRAIN EXTRACTS USED FOR SENSITIZATION

In table 1 is listed a group of 399 animals with which we determined the potency of the extracts derived from the various raw grains. Extracts of rice and wheat proved to be the most potent antigens, with

5. This feed contained cod liver oil, yeast, dried buttermilk, wheat germ middlings, linseed oil meal, rolled oat groats, wheat bran, crimped whole barley, alfalfa meal, crimped whole oats, molasses, cracked yellow corn, calcium carbonate, bone meal and iodized salt. The exact quantities of the various ingredients were not made known to us, but the major portion of the feed seemed to be rolled oats.

rye next in order. Corn was moderate in antigenic activity. On the other hand, barley extracts seemed to be of low potency. The same may be said of oats, but in this instance the factor of possible immunity established by the previous diet must be borne in mind. We believe, therefore, that the extracts used in these experiments, particularly those of rice, wheat, rye and corn, are potent allergens.

In determining the anaphylactogenicity of the cooked foods, only the animals which were shown to be sensitive to the homologous raw grain were used for evaluating the reduction in antigenicity.

HEATED GRAIN EXTRACTS USED FOR SENSITIZATION

An attempt was made to determine whether any modification in sensitizing capacity was evidenced by the cooked product. The data listed in table 2 appear to show that a marked reduction does occur.

TABLE 2.—*Anaphylactic Test Made with Alkaline Extracts of Cooked Wheat to Determine Its Sensitizing and Shocking Ability* *

Number of Animals	Sensitization with Cooked Wheat, Cc.	Shock with Cooked Wheat	Number of Animals	Sensitization with Cooked Wheat, Cc.	Shock with Cooked Wheat
28.....	3	0	10.....	15	0
2.....	3	+	7.....	15	+
4.....	10	0	2.....	15	++
1.....	10	++++	1.....	15	++++

* The sensitization dose was injected intraperitoneally; the shock dose was 0.5 cc., given intravenously. 0 indicates negative reaction; +, dyspnea; ++, dyspnea and convulsions, and ++++, death resulting from anaphylactic reaction, with typically balooned lungs.

In 30 animals given injections of a primary dose of 3 cc. practically no sensitization was established. As the primary dose was increased to five times that amount, a few were sensitized, the majority, however, only to a moderate degree, although in 2 instances a high degree of sensitivity was established. The sensitivity produced by cooked foods is in no way comparable to that generally established with the raw material (table 1).

IS THERE ANY CHANGE IN SPECIFICITY OF THE COOKED PROTEIN?

It has been suggested by Furth [6] and others that heated antigens have a specificity different from that of antigens in the homologous raw form. For this reason, animals were sensitized with the heated wheat, and attempts were made to cross shock with the homologous raw product. This was followed by a control shock dose with the heated material that had been used for sensitization. In table 3 it is noted that in only

6. Furth, J.: On Anaphylaxis with Heated Serum, J. Immunol. **11**:215, 1926.

3 of 19 animals studied was any sensitization obtained even after they had been sensitized with large amounts of heated material. In no instance was a shock reaction encountered with the heated material when the raw material gave a negative reaction. If any change in specificity results from moist heat, we were unable to demonstrate it in these experiments.

TABLE 3.—*Test Made for Cross Reactions with Cooked and with Raw Wheat to Determine if There Is Any Change in Specificity Results from Heating* *

Number of Animals	Sensitization with Cooked Wheat, Cc.†	Cross Shock with Raw Wheat	Control Shock with Material Used for Sensitization
10	3	0	0
4	10	0	0
1	10	++++	..
2	15	0	0
1	15	++	..
1	15	++++	..

* All shock doses contained 0.5 cc., administered intravenously; all control shock doses, 0.5 cc., were given intravenously one hour later.
† Cooked for twenty minutes under steam pressure at 240 F.

TABLE 4.—*Comparison of Results of Protein Tests and Nitrogen Determinations on Extracts of Raw Wheat and of Cooked Wheat*

Material	Protein Tests			Nitrogen Determination	
	Biuret	Millon	Hopkins-Cole	Kjeldahl Nitrogen, Mg. Per 100 Cc.	Nonprotein Nitrogen, Mg. Per 100 Cc.
Raw Farina	Strong Positive	Strong Positive	Positive	72	10
Cooked Farina*	Negative	Negative	Negative	26	0

* Cooked for twenty minutes under steam pressure at 240 F.

IS THERE REDUCTION IN ANTIGENIC CONTENT OF EXTRACTS OF COOKED GRAINS?

In table 4 is noted absence of protein reactions and striking reduction in the nitrogen content of an extract derived from a cooked product as compared with an extract made from the raw grain. The majority of the filtered extracts of cooked grains gave negative or only suggestive reactions. The filtered extracts of the raw grains which were used to sensitize the animals (wheat, rice, rye, corn, barley and oats) all gave positive results with the tests for protein (biuret, Millon's, Hopkins-Cole). The fact that the nitrogen content is reduced and that the protein reactions are weak or absent might in itself lead one to

the conclusion that there is reduction of antigenicity in the cooked product. However, minute amounts of antigen capable of eliciting hypersensitive reactions may not be demonstrable by chemical methods. We deemed it necessary, therefore, to pursue this work further by using the more delicate immunologic test.

In the course of experiments to determine whether or not the proteins of milk were altered during the process of evaporation in the preparation of commercial evaporated milk, Cutler [7] found that the quantity of soluble protein available from whey of evaporated milk was always less than half that obtained from raw milk, as determined by the Kjeldahl process.

The heating involved in the preparation of evaporated milk altered the immunologic properties of the whey proteins so that the minimum lethal dose was larger than that of the whey proteins from raw milk. Lewis and Hayden [8] also obtained by precipitation with trichloroacetic acid approximately half the amount of protein by weight from evaporated milk, as compared with that from raw milk. The quantitative reduction in the amount of protein in the filtrates of heated proteins suggests the reason that we could sensitize animals to lactalbumin with evaporated milk but were unable to induce shock with it.

Zinsser [9] found that with filtrates obtained from horse serum and crystalline egg albumin that had been subjected to prolonged boiling he obtained negative results with the ordinary qualitative tests for proteins, although they gave definitely positive reactions with the ring test and with the precipitin test. However, when this type of filtrate was evaporated over the free flame to one tenth or one twentieth of its original volume distinct qualitative protein reactions were obtained. The diminution in antigenicity of the filtrates obtained from heated products appears, therefore, to be due to the fact that coagulation by heat renders most of the antigen insoluble, that which remains in solution being insufficient to bring about protein reactions (table 4).

ALLERGENIC DENATURATION

The modification of antigenicity by heat which results from denaturation of some of the protein fractions raises several questions that should be discussed in order that the results of our experiments with heated grain foods may be better understood.

7. Cutler, O. I.: Antigenic Properties of Evaporated Milk, J. A. M. A. **92**: 964 (March 23) 1929.

8. Lewis, J. H., and Hayden, H. C.: Effect of Heat on the Antigenic Properties of Milk, Am. J. Dis. Child. **44**:1211 (Dec.) 1932.

9. Zinsser, H.: On Antigenic Properties of Horse Serum and Egg Albumin After Heat Coagulation, J. Immunol. **9**:227, 1924.

The early work of Besredka,[10] Rosenau and Anderson,[11] Kraus and Volk,[12] Doerr and Russ [13] and others demonstrated that heating various animal serums reduced their toxic properties but not their sensitizing ability. Spiegel-Adolf [14] found that the denaturation of serum albumin by heat can be reversed and that the recovered albumin is immunologically identical with the natural albumin. We [1] found that animals could be sensitized with denatured evaporated milk and shocked by purified lactalbumin derived from raw milk but that animals sensitized to lactalbumin from raw milk could not be shocked by evaporated milk.

In an effort to clarify the meaning of denaturation, which is variously interpreted, such qualifying terms as "light," "heat," "reversible" and "pseudo" have been prefixed to "denaturation." The term "heat denaturation" might be used to describe the change that occurs in cooked foods, but perhaps an even finer shade of distinction can be indicated by the term "allergenic denaturation."

By "allergenic denaturation" we mean the reduction of the shock-producing properties of an allergen. This change is brought about by the application of an adequate amount of moist heat to heat-labile proteins.

Whether the observed reduction in antigenic activity is due solely to removal from solution of antigenic fractions, as Zinsser [9] stated, or to a change in molecular configuration of the proteins still remaining in solution cannot be settled by the studies thus far made. (See Mirsky and Pauling [15] for a discussion of this phase.) The term "allergenic denaturation," therefore, is merely a term of biologic interest to connote the empiric observations that there is reduced antigenicity in certain foods or in other proteins when they are subjected to moist heat.

VARIOUS FORMS OF HEAT TO WHICH CEREAL GRAINS ARE SUBJECTED

It was of importance to know the character and amount of heat that is used in the preparation of some of the products discussed in the

10. Besredka, A.: Du méchanisme de l'anaphylaxie vis-à-vis du sérum de cheval, Ann. Inst. Pasteur **22**:496, 1908.

11. Rosenau, M. J., and Anderson, J. F.: Further Studies upon Anaphylaxis, Hygienic Laboratory Bulletin 45, United States Public Health Service, 1908.

12. Kraus, R., and Volk, R.: Zur Frage der Serumanaphylaxie, Ztschr. f. Immunitätsforsch. u. exper. Therap. **1**:731, 1908-1909.

13. Doerr, R., and Russ, V. K.: Studien über Anaphylaxie, Ztschr. f. Immunitätsforsch. u. exper. Therap. **3**:706, 1909.

14. Spiegel-Adolf, M.: Hitzeveränderungen des Albumins, Biochem. Ztschr. **170**:126, 1926.

15. Mirsky, A. E., and Pauling, L.: On the Structure of Native, Denatured and Coagulated Proteins, Proc. Nat. Acad. Sc. **22**:439, 1936.

present paper. Certain prepared cereals are subjected to two stages of heat in their manufacture. In the first stage, they are variously subjected to 10 to 22 pounds (4.5 to 10 Kg.) of steam pressure (at 240 to 262 F.) for anywhere from twenty minutes to three hours. These products which have been subjected to moist heat are then dry heated either on heated drums or in ovens at temperatures ranging from 200 to 430 F. for a few seconds to three quarters of an hour.

The dry cereal products, such as Melba toast, bread, cookies, sponge-cake and piecrust, are heated at oven temperatures of from 325 to 500 F. for from ten minutes to three quarters of an hour. Bread is baked in an oven at 450 F. for forty to forty-five minutes. This heat, however, does not penetrate, and the inside temperature of the loaf never is higher than 200 to 212 F. On the other hand, Melba toast, which is bread cut very thin, gets a second and a third heating at approximately the same temperature, and in this instance apparently the heat actually penetrates the mass. Cookies and pastries are dry heated for only ten minutes.

The home-cooked cereals have no standardized methods and are variously kept at boiling temperatures for anywhere from five minutes to three hours.

Thus it is obvious that the heat applied to the various forms of grain foods varies not only in type, i. e., moist or dry, but in length of time applied as well as in degree.

ANAPHYLACTOGENIC PROPERTIES OF CEREAL FOODS

The protocols of the experiments on which the following general conclusions are based (table 6) appear at the end of the article. The results of 546 animal experiments are included in these protocols.

Prepared Dry Cereals.—The results with these products were contrary to our expectations, which were based on our experience with dry milk. The drying of milk is accomplished by a single process of dehydration, which does not reduce its antigenicity. The dry cereal preparations, however, are subjected to 10 to 22 pounds of steam pressure for periods ranging from one half hour to several hours before being dehydrated; actually, therefore, they have been denatured by moist heat in the first stage, and the drying process is secondary. The antigenic potencies of many of these manufactured products have been reduced, to a large extent, and the foods may be regarded as allergenically denatured.

Cooked Cereals.—Farina and rolled oatmeal cooked in a double boiler for from one to three hours apparently lose their ability to shock sensitized animals. Boiled corn meal and boiled rice, however, retain their anaphylactogenicity.

One must bear in mind that unless specific directions for the preparation of such cereals in the home are given and carried out there is an element of uncertainty as to the degree of heat applied and the actual length of time the cereal is cooked.

Cereal Pastes.—Under this head we include such foods as spaghetti, macaroni and noodles, which are subjected to a moderate degree of dry heat in their manufacture. According to directions, they require cooking for ten minutes in boiling water. Despite the fact that they are cooked for so short a time, they appear to be allergenically denatured. It may be that the protein elements are prevented from going into solution because they are masked by swollen starch granules.

Crackers.—All forms of biscuits, crackers, cookies, matzoths, pretzels and zwieback which we tested were anaphylactogenic. This form of breadstuff is usually baked for about ten minutes at an oven temperature ranging from 375 to 400 F. The short exposure to dry heat is apparently insufficient to bring about antigenic changes.

Cereals Containing Several Grains.—In a certain specially prepared cereal for infants approximately 50 per cent of the total content is wheat, smaller amounts of corn and oats being present. Their antigenic potency is reduced, and they were tolerated by animals sensitized to wheat, corn and oat.

Pancake flours contain wheat, rye, corn, rice and other grains, none of which is denatured either in manufacture or in the cooking processes to which it is subjected.

Bread.—Bread is anaphylactogenic. Ordinary bread is baked forty to forty-five minutes at an oven temperature of 450 F. While the crust is at approximately the same temperature as the oven, the inside temperature of the loaf is only from 200 to 212 F.

Melba toast, that is, bread which is thinly sliced and thoroughly oven dried, is nonanaphylactogenic. Other forms of toast retain their antigenicity.

Cakes and Pastries.—Cakes and pastries are cooked at a relatively low temperature for a moderate period with dry heat. They retain their anaphylactogenic powers.

Puddings.—Corn starch and rice puddings are anaphylactogenic.

Waffles and Pancakes.—These are anaphylactogenic.

Corn Foods.—Popcorn and corn syrup are allergenically denatured, whereas corn on the cob, canned corn, corn fritters, corn pudding and corn breads are all anaphylactogenic.

Interrelation of Rye and Wheat.—Wells and Osborne[3] originally pointed out the fact that the gliadins of wheat and rye are chemically and biologically related. We corroborated this by sensitizing animals

to raw wheat and shocking them with rye and, conversely, by sensitizing with rye and shocking with wheat. It is interesting that a certain rye biscuit did not shock wheat-sensitized animals but did shock rye-sensitized animals. This seems to indicate that the common factor in rye and wheat is present in rather small amounts and that this common fraction may be more easily denatured by heat than the other protein fractions in these grains.

TABLE 5.—*Classification of Cooked Cereal Foods and Breadstuffs According to Their Anaphylactogenicity* *

Allergenic		Allergenically Denatured	
Wheat		**Wheat**	
White bread	Pretzels	Multiple precooked dry cereal	Spaghetti, macaroni, noodles†
Rye bread	Matzoths	Various precooked wheat cereals	Melba toast
Ordinary toast	Waffles	Wheat and multiple cereals cooked in a double boiler†	Rye biscuit
Zwieback	Pancakes		Dextrimaltose
Crackers (all varieties)	Cakes (all forms)		Wheat and multiple cereals cooked in a double boiler†
Cookies (all varieties)	Piecrust		
	Pastries		
Rye		**Rye**	
Sour rye bread	Swedish rye bread		
Ordinary rye bread	Rye biscuit		
Pumpernickel	Pancakes		
Corn		**Corn**	
Cooked corn meal	Corn fritters	Precooked corn cereals	Popcorn
Canned corn	Pancakes		Corn syrup
Corn on cob	Corn breads		
Corn starch pudding			
Rice		**Rice**	
Boiled rice	Pancakes	Precooked rice cereal B	Cooked brown rice†
Rice pudding	Rice fritters		
Precooked rice cereal A	Rice cookies		
	Rice cakes		
Barley		**Barley**	
Malt extracts and brews	Pearled barley	Dextrimaltose	
Malted cereals	Barley water		
Malted milk preparations			

* We were unable to sensitize animals with oat. Oat products, therefore, are not included in this chart.

† The unstandardized methods of preparation of home-cooked products militates against their use by the exquisitely sensitive person.

Malt Extracts.—Malt extracts and malted beverages retain their anaphylactogenicity, as was shown in a previous paper.[16]

Résumé.—The data in table 5 show which of these cooked grain foods are allergenically denatured and which are not. This classification is based entirely on the anaphylaxis test with the guinea pig.

16. Ratner, B., and Gruehl, H. L.: Anaphylactogenic Properties of Malted Sugars and Corn Syrup, Am. J. Dis. Child. **49**:307 (Feb.) 1935.

COMMENT

In the present state of knowledge, it is impossible to predict the antigenic behavior of the various heated foods. For example, one could not foretell that dry milks retain their antigenicity whereas heated liquid milks have to a large extent lost this property and that dry dextrimaltose preparations are not anaphylactogenic whereas the liquid malt extracts are. In general, it appears that the coagulable protein fractions subjected to relatively high temperatures in the presence of moisture undergo a change which results in allergenic denaturation. Yet certain forms of food proteins, e. g., casein,[17] almond, oat and ovomucoid,[18] soy bean[19] and fish,[20] appear to be extremely resistant to high temperatures, even in the presence of moisture, and retain their antigenic properties, as determined both in man and in animals.

Chick and Martin[21] showed that the coagulation of hemoglobin and egg albumin by heat is not an instantaneous process but proceeds with definite velocity and increases markedly with a rise in temperature. This suggests the reason, at least in part, for the difference in results obtained with the variously heat-treated grain products. However, in all probability the chemical composition of the various proteins is the principal factor which determines their ability to be denatured by heat.

In the experiments reported in this study, the various forms of cereal products were subjected to varying degrees and types of heat, unlike the uniform temperature of 116 C. to which evaporated milk is subjected. In some instances, cereal grains were heated to 10 (4.5 Kg.) pounds of steam pressure for twenty minutes; in other instances, they were treated with 22 pounds (10 Kg.) of steam pressure for as long as an hour or more. Then again, breads and crackers were baked by dry oven heat from ten minutes to three quarters of an hour.

Our protocols (table 6) show that in many instances products retained their antigenicity in spite of being heated, which indicates that there are relative differences in the antigenicity of the cooked grain foods.

Schloss[18] found that heated oat retained its skin-sensitizing capacity. It was impossible for us to arrive at any conclusions relative to oats because of the refractoriness of the animals.

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17. Wells, H. G., and Osborne, T. B.: Anaphylaxis Reactions with Purified Proteins from Milk, J. Infect. Dis. **29**:200, 1921.

18. Schloss, O. M.: A Case of Allergy to Common Foods, Am. J. Dis. Child. **3**:341 (June) 1912.

19. Duke, W. W.: Soy Bean as a Possible Important Source of Allergy, J. Allergy **5**:300, 1934.

20. Prausnitz, C., and Küstner, H.: Studien über die Ueberempfindlichkeit, Centralbl. f. Bakt. (Abt. 1) **86**:160, 1921.

21. Chick, H., and Martin, C. J.: On the "Heat Coagulation" of Proteins, J. Physiol. **40**:404, 1910.

It would have been beyond the scope of this study to analyze the antigenicity of each of the protein fractions of the various grains or to make precipitin determinations. We were concerned with the grain products as they are consumed by the human being and not with purified proteins. The anaphylactic method seemed to be the most sensitive and direct procedure for determining the relative antigenicity of such foods.

Studies on the influence of heat on proteins thus far seem to indicate that antigenic changes are dependent on (1) the type, duration and degree of heat used and (2) the type of protein studied. The rapidity and completeness of the coagulation of the protein determine the degree of residual antigenicity due to the operation of these two factors.

A point of further interest is the relation that heat has to the digestibility of protein. Mendel and Lewis [22] and Bateman [23] showed that raw egg white is digested only to a small extent, whereas cooked egg white is digested to a greater degree. Furthermore, Hess, Koch and Sennewald [24] and Wallen-Lawrence and Koch [25] showed that boiled or evaporated milks are more readily digested in vitro by pepsin and trypsin than raw milk, the changes being quantitative in proportion to the amount of heat applied and the length of time of heating. Since no change is noted in the digestibility of casein after prolonged heating, it is assumed that the increase in digestibility is due to a change in some heat-labile constituent in the whey. This may suggest that heat-labile food proteins, in general, are more rapidly digested into harmless split products, which when absorbed are not toxic, whereas in the digestion of raw food proteins or those which are not heated sufficiently the undigested particles may act as antigens when absorbed. The reduced antigenicity determined by intravenous injection in the sensitized guinea pig therefore raises the presumption that certain heated food products can be tolerated by the specifically sensitive human being.

Clinical experience will have to be the final criterion in the decision whether the results obtained with lower animals can be applied in cases of hypersensitivity to a specific food in human beings. It is possible that one may not be able to use a particular cereal food which has been found to be allergenically denatured for persons who are exquisitely sensitive. In our animal experiments, certain animals gave

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moderate reactions to the allergenically denatured forms, whereas the majority were unaffected. So with human subjects individual differences must be taken into account, as well as the fact that the coagulable protein fractions withstand the most energetic treatment by heat without completely losing their ability to react with antibodies. This may have considerable bearing on what actually takes place in the intestinal tract of a particularly sensitive person.

We have learned that such products as bread, toast, zwieback, crackers, biscuits, pancakes, waffles, pastries, cakes, piecrust and the majority of corn products cannot be tolerated by the specifically sensitized guinea pig. On the other hand, certain commercially precooked dry cereals are reduced in their antigenicity and produce little or no reaction in sensitized animals. With home-cooked products uncertainty exists chiefly because of the lack of standardization of preparation in the home.

The methods used in these experiments have no counterpart, of course, in the spontaneous sensitization of human beings to grain foods. The purposeful exaggeration of the methods used, nevertheless, has afforded us an opportunity to determine with a certain degree of accuracy whether there is modification in antigenicity of cooked grain foods.

We believe that these results of experiments with the guinea pig may be translated into terms of allergy in man and applied to the problem of the allergic person hypersensitive to cereal grains.

SUMMARY AND CONCLUSIONS

Certain grain products subjected to moist heat undergo a change which results in allergenic denaturation. This term is suggested to connote the empiric observation that there is reduced antigenicity in certain food proteins which have been subjected to moist heat.

The effect that heat has on the antigenicity of food products depends, first, on the heat stability or heat lability of the different molecular components and, second, on the length of time they are heated and the type and degree of heat used.

Animals have been sensitized with raw cereal grains and tested with homologous cooked products. A classification of cooked cereal foods and breadstuffs shows those which are allergenically denatured and those which are not.

On the basis of analogy with the animal experiments reported here, we believe that it is not unreasonable to conclude that certain heat-treated grain foods may be used in selected cases of allergy. Diets free from wheat and from other grains should be revised to include the allergenically denatured foods described. Their incorporation in the diets of persons sensitive to foods will aid in establishing better nutrition and avert the introduction of psychologic feeding problems.

TABLE 6.—*Protocols of Experiments Showing Anaphylactogenic Properties of Cereal Foods* *

Sensitization with Wheat

Animal	Shock Multiple Precooked Dry Cereal	Control Shock Wheat	Animal	Shock Multiple Precooked Dry Cereal	Control Shock Wheat
1	0	0	11	0	+++
2	0	0	12	0	++++
3	0	+	13	0	++++
4	0	+	14	0	++++
5	0	+	15	0	++++
6	0	+	16	0	++++
7	0	+	17	0	++++
8	0	+	18	+	+
9	0	++	19	+	++++
10	0	++			

Sensitization with Wheat Germ

Animal	Shock Multiple Precooked Dry Cereal	Control Shock Wheat Germ	Animal	Shock Multiple Precooked Dry Cereal	Control Shock Wheat Germ
20	0	0	24	0	++++
21	0	0	25	+	++++
22	0	+++	26	+	++++
23	0	+++	27	+	++++

Sensitization with Wheat

Animal	Shock Multiple Precooked Dry Cereal	Control Shock Yeast	Animal	Shock Multiple Precooked Dry Cereal	Control Shock Yeast
28	0	0	31	0	+
29	0	0	32	0	+
30	0	+			

Sensitization with Corn

Animal	Shock Multiple Precooked Dry Cereal	Control Shock Corn	Animal	Shock Multiple Precooked Dry Cereal	Control Shock Corn
33	0	0	42	0	++
34	0	0	43	0	++
35	0	0	44	0	+++
36	0	0	45	0	+++
37	0	0	46	0	+++
38	0	+	47	0	++++
39	0	+	48	0	++++
40	0	+	49	0	++++
41	0	+	50	0	++++

Sensitization with Oat

Animal	Shock Multiple Precooked Dry Cereal	Control Shock Oat	Animal	Shock Multiple Precooked Dry Cereal	Control Shock Oat
51	0	0	59	0	0
52	0	0	60	0	+
53	0	0	61	0	+
54	0	0	62	0	+
55	0	0	63	0	+
56	0	0	64	0	+
57	0	0	65	0	+
58	0	0	66	0	+

Sensitization with Wheat

Animal	Shock Cooked Farina (1 Hr.)	Control Shock Wheat	Animal	Shock Cooked Farina (1 Hr.)	Control Shock Wheat
67	0	++	72	0	++++
68	0	+++	73	0	++++
69	0	+++	74	0	++++
70	0	+++	75	+	++
71	0	++++	76	+	++++

	Cooked Farina (3 Hr.)	Wheat		Cooked Farina (3 Hr.)	Wheat
77	0	+	82	0	++
78	0	+	83	0	++++
79	0	++	84	0	++++
80	0	++	85	0	++++
81	0	+++	86	0	++++

TABLE 6.—*Protocols of Experiments Showing Anaphylactogenic Properties of Cereal Foods*—Continued*

	Cooked Multiple Cereal (1 Hr.)	Wheat		Cooked Multiple Cereal (1 Hr.)	Wheat
87	0	0	92	0	+++
88	0	+	93	0	+++
89	0	+	94	0	++++
90	0	+	95	+	+
91	0	++	96	+	++++
	Precooked Wheat Cereal A	**Wheat**		**Precooked Wheat Cereal A**	**Wheat**
97	0	+	102	0	++++
98	0	+++	103	+	++
99	0	+++	104	+	+
100	0	++++	105	+	+++
101	0	++++	106	+	+++
	Precooked Wheat Cereal B	**Wheat**		**Precooked Wheat Cereal B**	**Wheat**
107	0	0	112	0	+++
108	0	0	113	0	+++
109	0	+	114	0	++++
110	0	++	115	+	++
111	0	++	116	+	+++
	Precooked Wheat Cereal C	**Wheat**		**Precooked Wheat Cereal C**	**Wheat**
117	0	0	122	0	+++
118	0	0	123	0	++++
119	0	0	124	0	++++
120	0	++	125	0	++++
121	0	++	126	0	++++
	Precooked Wheat Cereal D	**Wheat**		**Precooked Wheat Cereal D**	**Wheat**
127	0	0	132	0	++++
128	0	0	133	0	++++
129	0	0	134	0	++++
130	0	++++	135	0	++++
131	0	++++	136	+	++++
	Precooked Wheat Cereal E	**Wheat**		**Precooked Wheat Cereal E**	**Wheat**
137	0	0	142	0	++
138	0	0	143	0	++++
139	0	0	144	0	++++
140	0	0	145	0	++++
141	0	++	146	0	++++
	Melba Toast	**Wheat**		**Melba Toast**	**Wheat**
147	0	0	152	0	+++
148	0	+	153	0	+++
149	0	++	154	0	++++
150	0	+++	155	0	++++
151	0	+++	156	+	++++
	Whole Wheat Crackers	**Wheat**		**Whole Wheat Crackers**	**Wheat**
157	0	0	162	0	++++
158	0	+	163	0	++++
159	0	++	164	+	++
160	0	+++	165	+	++++
161	0	+++	166	+	++++
	Cooked Spaghetti	**Wheat**		**Cooked Spaghetti**	**Wheat**
167	0	+	174	0	++++
168	0	+++	175	+	+
169	0	+++	176	+	+++
170	0	++++	177	+	+++
171	0	++++	178	+	+++
172	0	++++	179	+	++++
173	0	++++	180	+	++++
	Rye Flour	**Wheat**		**Rye Flour**	**Wheat**
181	0	0	186	+++	+++
182	0	+++	187	+++	+++
183	0	++++	188	+++	++++
184	0	++++	189	++++	
185	+	++++	190	++++	

TABLE 6.—*Protocols of Experiments Showing Anaphylactogenic Properties of Cereal Foods*—Continued*

	Rye Biscuit	Wheat		Rye Biscuit	Wheat
191	0	0	194	0	+++
192	0	+	195	0	++++
193	0	++	196	0	++++
	White Bread	**Wheat**		**White Bread**	**Wheat**
197	0	0	202	++	++
198	0	0	203	+++	+++
199	0	0	204	++++	
200	++	++	205	++++	
201	++	++	206	++++	
	Ordinary Toast	**Wheat**		**Ordinary Toast**	**Wheat**
207	0	++	212	+	+
208	0	++	213	+	+
209	0	++	214	+	+
210	0	++	215	+	++
211	+	+	216	+	++
	Rye Bread	**Wheat**		**Rye Bread**	**Wheat**
217	0	0	222	++	++++
218	0	0	223	+++	++++
219	0	0	224	+++	++++
220	+	++	225	++++	
221	++	++++	226	++++	
	Zwieback	**Wheat**		**Zwieback**	**Wheat**
227	0	0	232	++	++++
228	0	0	233	++	++++
229	0	+	234	++	++++
230	0	+++	235	+++	+++
231	++	+++	236	++++	
	Soda Biscuit	**Wheat**		**Soda Biscuit**	**Wheat**
237	++	+++	242	++++	
238	++	+++	243	++++	
239	+++	+++	244	++++	
240	+++	+++	245	++++	
241	+++	++++	246	++++	
	Sugar Cookie	**Wheat**		**Sugar Cookie**	**Wheat**
247	0	0	252	++	++++
248	0	0	253	+++	++++
249	+	+	254	+++	++++
250	+	+	255	++++	
251	++	++++	256	++++	
	Butter Cracker	**Wheat**		**Butter Cracker**	**Wheat**
257	0	0	262	++	++
258	0	0	263	+++	+++
259	+	+++	264	+++	+++
260	+	+++	265	+++	+++
261	++	++	266	+++	+++
	Pretzel	**Wheat**		**Pretzel**	**Wheat**
267	0	0	272	++	+++
268	0	0	273	+++	+++
269	+	+	274	+++	+++
270	+	+	275	+++	++++
271	++	+++	276	+++	++++
	Matzoth	**Wheat**		**Matzoth**	**Wheat**
277	+	+	283	+++	+++
278	+	+	284	+++	+++
279	+	+	285	++++	
280	++	++	286	++++	
281	++	++			
282	+++	+++			
	Waffle	**Wheat**		**Waffle**	**Wheat**
287	0	0	292	+	++
288	0	0	293	++	++
289	0	0	294	++	++
290	0	+	295	++	++++
291	+	+	296	++	++++

TABLE 6.—*Protocols of Experiments Showing Anaphylactogenic Properties of Cereal Foods*—Continued*

	Pancake	Wheat		Pancake	Wheat
297	0	++++	302	++	++++
298	+	+++	303	+++	+++
299	+	+++	304	+++	+++
300	+	++++	305	+++	++++
301	++	++	306	++++	
	Spongecake	**Wheat**		**Spongecake**	**Wheat**
307	+	+	312	+++	+++
308	+	+	313	+++	+++
309	++	++	314	+++	+++
310	++	++	315	++++	
311	+++	+++	316	++++	
	Piecrust	**Wheat**		**Piecrust**	**Wheat**
317	+	+++	322	++	+++
318	+	+++	323	++	++++
319	++	++	324	++	++++
320	++	++	325	+++	+++
321	++	+++	326	+++	+++
		Sensitization with Rye			
	Raw Wheat	**Rye**		**Raw Wheat**	**Rye**
327	+	+	332	+++	++++
328	+	+	333	++++	
329	++	++	334	++++	
330	++	++	335	++++	
331	+++	++++	336	++++	
	Rye Bread	**Rye**		**Rye Bread**	**Rye**
337	0	0	342	+	++
338	0	0	343	+	+++
339	0	0	344	+	+++
340	+	++	345	+	++++
341	+	++	346	+	++++
	Pumpernickel	**Rye**		**Pumpernickel**	**Rye**
347	0	0	352	++	++
348	0	0	353	++	++
349	+	+	354	+++	+++
350	+	+	355	+++	+++
351	+	+	356	+++	+++
	Rye Biscuit	**Rye**		**Rye Biscuit**	**Rye**
357	0	0	362	+	+++
358	0	+	363	+	+++
359	0	+	364	++	++
360	0	+++	365	++	+++
361	0	+++	366	++	+++
		Sensitization with Rice			
	Boiled Rice (½ Hr.)	**Rice**		**Boiled Rice (½ Hr.)**	**Rice**
367	0	+++	372	+	++
368	0	+++	373	+	+++
369	0	+++	374	+	+++
370	0	+++	375	+	++++
371	+	++	376	+	++++
	Boiled Brown Rice (40 Min.)	**Rice**		**Boiled Brown Rice (40 Min.)**	**Rice**
377	0	0	382	0	++
378	0	0	383	0	+++
379	0	+	384	0	+++
380	0	+	385	0	+++
381	0	++	386	0	+++
	Baked Rice Pudding	**Rice**		**Baked Rice Pudding**	**Rice**
387	0	0	392	+	+++
388	0	0	393	+	++++
389	+	+++	394	+	++++
390	+	+++	395	+	++++
391	+	+++	396	+	++++

TABLE 6.—*Protocols of Experiments Showing Anaphylactogenic Properties of Cereal Foods*—Continued*

	Precooked Rice Cereal A	Rice		Precooked Rice Cereal A	Rice
397	0	++	402	0	++++
398	0	++	403	+	+++
399	0	++	404	+	+++
400	0	++	405	+	++++
401	0	++++	406	+	++++
	Precooked Rice Cereal B	**Rice**		**Precooked Rice Cereal B**	**Rice**
407	0	+++	412	0	+++
408	0	+++	413	0	++++
409	0	+++	414	0	++++
410	0	+++	415	+	+++
411	0	+++	416	+	+++
	Pancake	**Rice**		**Pancake**	**Rice**
417	0	+++	422	0	+++
418	0	+++	423	+	+++
419	0	+++	424	+	+++
420	0	+++	425	+	+++
421	0	+++	426	+	+++
		Sensitization with Corn			
	Boiled Corn Meal (2 Hr.)	**Corn**		**Boiled Corn Meal (2 Hr.)**	**Corn**
427	0	0	432	0	++
428	0	0	433	+	+
429	0	+	434	+	+
430	0	+	435	+	++
431	0	++	436	+	++
	Cooked Multiple Cereal (1 Hr.)	**Corn**		**Cooked Multiple Cereal (1 Hr.)**	**Corn**
437	0	0	442	0	+++
438	0	0	443	0	+++
439	0	+	444	0	+++
440	0	+	445	0	+++
441	0	+++	446	0	+++
	Canned Corn	**Corn**		**Canned Corn**	**Corn**
447	0	0	452	0	+++
448	0	0	453	+	++
449	0	++	454	+	++
450	0	++	455	+	+++
451	0	++	456	++	++
	Corn Starch Pudding	**Corn**		**Corn Starch Pudding**	**Corn**
457	0	0	462	0	0
458	0	0	463	+	+
459	0	0	464	+	+
460	0	0	465	+	+
461	0	0	466	+	++
	Pancake	**Corn**		**Pancake**	**Corn**
467	0	0	472	0	0
468	0	0	473	+	++
469	0	0	474	+	++
470	0	0	475	+	++
471	0	0	476	+	++
	Corn Muffin	**Corn**		**Corn Muffin**	**Corn**
477	0	0	482	0	0
478	0	0	483	0	+
479	0	0	484	+	+
480	0	0	485	+	++
481	0	0	486	+	+++
	Popcorn	**Corn**		**Popcorn**	**Corn**
487	0	0	492	0	+
488	0	0	493	0	+
489	0	0	494	0	+++
490	0	+	495	0	+++
491	0	+	496	0	+++

TABLE 6.—*Protocols of Experiments Showing Anaphylactogenic Properties of Cereal Foods*—Continued*

	Precooked Corn Cereal A	Corn		Precooked Corn Cereal A	Corn
497	0	+	502	0	+
498	0	+	503	0	++
499	0	+	504	0	++
500	0	+	505	0	++
501	0	+	506	0	++
		Barley Sensitization			
	Boiled Barley (20 Min.)	Barley		Boiled Barley (20 Min.)	Barley
507	0	0	512	0	0
508	0	0	513	0	0
509	0	0	514	0	0
510	0	0	515	0	0
511	0	0	516	0	0
	Malt Extracts	Barley		Malt Extracts	Barley
517	0	0	522	0	+
518	0	0	523	+	+
519	0	0	524	+	+
520	0	0	525	+	+++
521	0	+	526	+	+++
	Malted Drinks	Barley		Malted Drinks	Barley
527	0	0	532	0	0
528	0	0	533	+	+
529	0	0	534	+	+
530	0	0	535	+	+
531	0	0	536	+	+
	Precooked Malted Cereal A	Barley		Precooked Malted Cereal A	Barley
537	0	0	542	0	0
538	0	0	543	0	0
539	0	0	544	0	0
540	0	0	545	0	0
541	0	0	546	0	0

* All animals were sensitized with 10 cc. of an alkaline extract of raw grain injected intraperitoneally. All shock injections were made intravenously with 0.5 cc. of an alkaline extract of the particular substance tested. All control shock injections were made intravenously with 0.5 cc. of an alkaline extract of the same substance used for sensitization.

In the table ++++ indicates lethal anaphylaxis; +++, dyspnea, convulsions and collapse with recovery; ++, dyspnea and convulsions; +, severe dyspnea, and 0, negative reaction.

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SCARLET FEVER, HEMOLYTIC STREPTOCOCCIC CULTURES AND DICK TESTS IN A CHILDREN'S HOSPITAL

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PREFACE

The circumstances surrounding the publication of this paper call for an introduction. It constitutes a final report on an extensive investigation initiated by the late Dr. Silber C. Peacock. The work was carried out by him and by Miss Marie Werner throughout 1934 and 1935 and was completed in the two years following Dr. Peacock's death (on Jan. 3, 1936) by Dr. J. A. Bigler and Miss Werner. The investigation was a search for light on the incidence, distribution, specificity and clinical significance—in short, the epidemiology—of the hemolytic streptococcus and on its relation to scarlet fever, as revealed in a study of all of the personnel of the Children's Memorial Hospital and of all of the patients, both while they were in the hospital and after their discharge. Dr. Peacock had planned to carry on this line of investigation indefinitely. This plan was cut short by his tragic and untimely death. He was a keenly meticulous and methodical worker, with an uncanny sense and an unending enthusiasm for gathering statistical information. The data that he and Miss Werner had gathered were therefore in such order that they could be accurately formulated and correlated and the work itself could be carried on to its present state of completion by Dr. Bigler and Miss Werner. While all of the authors shared more or less equally in the undertaking, there was always back of it the sentiment that its presentation should stand as a final tribute to Dr. Peacock from both the Children's Memorial Hospital and the Otho S. A. Sprague Memorial Institute.

JOSEPH BRENNEMANN, M.D.

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1. CULTURES FOR HEMOLYTIC STREPTOCOCCI OF MATERIAL FROM HOSPITAL PERSONNEL AND PATIENTS

During the latter part of 1933 scarlet fever developed in an unusually large number of the personnel and patients of the Children's Memorial

† Dr. Peacock died on Jan. 3, 1936.

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From the Otho S. A. Sprague Memorial Institute Laboratory and the Children's Memorial Hospital.

Hospital. It was thought that a study of both personnel and patients might curb this situation and that if it were coupled with a review of all the cases of scarlet fever which developed in Chicago over a like period it might bring out some facts concerning the epidemiology of the disease.

This intensive investigation was carried out during 1934 and 1935 and during the first months of 1936. The personnel included not only nurses, interns and staff doctors, who were in contact with patients, but other employees of the hospital, such as dietitians and laundry and household workers.

Cultures of material from the nose and throat for hemolytic streptococci and Dick tests were made for all children who were admitted to the hospital. Similar cultures were made for all personnel, and Dick tests were made before employment. Cultures were made and Dick tests were performed for the whole hospital personnel at the beginning of the study, and repeated cultures were made for the whole group on several occasions thereafter. Material from the personnel of a general hospital was also cultured, and Dick tests were performed, these subjects serving as controls. Repeated cultures were often made for those who had had positive cultures. It was noted whether the throat was inflamed and whether the tonsils were present or had been removed. Dick tests were repeatedly performed on groups of patients with and without positive cultures. Frequently when scarlet fever developed in the hospital cultures were made for all possible contacts of the patient. All the cases of scarlet fever which occurred in Chicago in 1934 and 1935 were reviewed, and an effort was made to trace secondary infection to primary involvement in the same family, with relation to the time of onset of the disease. All this material has been correlated and will be presented under appropriate titles.

All the Dick tests, numbering several thousand, and all the culturing were performed by the same persons in order to eliminate, as far as possible, individual variations in interpretation.

This part of the study will deal only with the results of cultures for hemolytic streptococci of material from the noses and throats of the patients and personnel of a children's hospital and the personnel of a general hospital. The latter group should serve in a comparison of children and adults in regard to patient contact. The general hospital is a private hospital of the highest type, with a bed capacity of about 100. Nearly all of the patients are adults with such diseases as are encountered in any good private hospital. The Children's Memorial Hospital is a charity institution with a bed capacity of 252. Children ranging in age from after the newborn period to 13 years are admitted from the large outpatient department for all medical and surgical conditions except contagious diseases.

All cultures were made on blood agar plates by the usual method of swabbing the area from which material was to be taken and then streaking the plate. In reading the plates care was taken to eliminate other hemolytic colonies, such as hemolyzing staphylococci. As it was often impossible to count or even to estimate the number of colonies of hemolytic streptococci on a plate, percentages were used: less than 10 per cent, 10 to 50 per cent and 50 to 100 per cent, to designate roughly the amount of growth and the degree of hemolysis. Only in this way could we indicate to what degree a culture of material from the nose or throat was positive. By this arbitrary classification we do not mean to imply that a patient with a 10 per cent positive culture for hemolytic streptococci of material

from the throat is any less likely to transmit scarlet fever than one with a 100 per cent positive culture, and nothing in our study indicates that this is true.

From the whole personnel or from groups of the personnel of both the children's hospital and the general hospital material to be cultured was taken during one day at various times. Material to be cultured for the patients then resident in the children's hospital was also taken in this manner.

The dates and the results of these culture surveys are given in table 1. The percentage of positive cultures for the personnel groups of the children's hospital had a variation of from 3 to 6 per cent in the different surveys. The positive cultures for the personnel of the general hospital were about 3 per cent less than for the personnel of the children's hospital. These are small differences when the total number of negative cultures is considered. It would seem, then, that a member of the personnel of a children's hospital is not much more likely to have a

TABLE 1.—*Results of Cultures for Hemolytic Streptococci of Material from the Noses and Throats of Hospital Personnel and Patients*

	Personnel of General Hospital			Personnel of Children's Hospital						Patients of Children's Hospital		
		Identical Group, 1935				Identical Groups,* 1935		Identical Group, 1935			Identical Group, 1936	
	1934			1934						1934		
Dates	1/7	1/24	1/25	1/24	7/20	1/17	1/18	12/19	12/20	1/7	9/3	9/4
Number of subjects	150	133	133	383	306	323	194	186	186	124	115	115
Positive cultures	21	16	12	65	35	48	14	32	34	55	29	28
10% positive or less	5	7	5	30	27	30	11	16	17	28	11	9
10-50% positive	10	9	6	11	5	9	1	6	7	8	12	17
50-100% positive	6	0	1	24	3	9	2	10	10	19	6	2
Per cent positive	14	12	9.1	17	11.4	14.9	7	17	17.7	44.5	25	24

* Members of personnel from whom material for culture was taken on Jan. 18, 1935, had negative cultures of material taken on January 17.

positive hemolytic streptococcic culture of material from the nose and throat than one of the personnel of a general hospital, even though scarlet fever and infections of the upper respiratory tract are much more prevalent in children than in adults. The percentage of positive cultures varied little during 1934 and 1935, although it was moderately lower during the summer months. At the beginning of the survey, when scarlet fever was occurring in the Children's Memorial Hospital in many instances, only 17 per cent of the entire personnel had positive cultures for hemolytic streptococci, in contrast to positive cultures for 44.5 per cent of the patients resident in the hospital at that time.

Material for culture was taken from identical groups of personnel and patients on successive days. Although the percentage of positive cultures of material taken on each of the two days was usually the same, a fairly constant variation was found when the persons with positive cultures for each day were considered. Of the 323 members of personnel from whom material was taken on January 17, 15 per cent had positive

cultures. On the following day material was taken from 194, all with negative cultures of material taken the previous day, and for an additional 7 per cent cultures were positive. From 186 of the personnel material was taken on both December 19 and December 20, cultures for 32, or 17 per cent, and 34, or 17.7 per cent, respectively, being positive. Of those with positive cultures only 24 had positive cultures for both days, while 8 had positive cultures for the first day and negative for the next, and 10 had negative for the first day and positive for the next. From 133 of the personnel of the general hospital material was taken on two successive days, 16, or 12 per cent, having positive cultures for the first day and 12, or 9 per cent, for the second day. In comparing those with positive cultures, it was found that 8 had positive cultures for both days, 8 had positive cultures only for the first day, and 4 had negative cultures for the first day and positive for the second. Cultures of material taken on successive days from 115 patients in the Children's Memorial Hospital showed the same variation, 20 patients having positive cultures for both days, 9 only for the first day and 8 only for the second. From still another group, composed of 60 nurses and 42 patients, material for culture was taken daily for two weeks; approximately the same irregularity occurred, in that the cultures of a person would be positive or negative on different occasions. It would seem from this that too much reliance cannot be placed on a negative culture of material taken on any one day when carriers of hemolytic streptococci are considered.

When cultures were made for the patients resident in the children's hospital with material taken on Jan. 7, 1934, it was found that 44.5 per cent of the subjects had positive cultures for hemolytic streptococci. This occurred during the period when scarlet fever was occurring in so many hospital patients. This high incidence of positive cultures is in sharp contrast to the incidence of 17 per cent for the hospital personnel at that time, and it is much higher than was ever subsequently found in later culture surveys of hospital patients. It was found that practically all the patients in an open ward had positive cultures. With isolation and other precautions the number of patients with positive cultures was reduced to about 25 per cent, as shown in the culture survey of September 1936. Even this is higher than the incidence of 19.2 per cent, which was the average for all patients when they were admitted to the hospital during the period of study. This increase of positive cultures for patients after they were resident in the hospital may be due to several factors. In the surveys of hospital patients those admitted for tonsillectomy only were not included. Patients that were admitted during months when the incidence of positive cultures was high were in contact with patients then resident in the hospital who had negative

cultures. In addition, there was always the contact with sick patients and with those caring for the sick. The usual culture medium for the hemolytic streptococcus was blood agar. By this simple method differentiation of the various strains of the hemolytic streptococcus is not possible, and one does not know whether a positive culture is made up of strains that are generally accepted as the cause of scarlet fever or strains which may cause other streptococcic diseases. If scarlet fever is spread by contact, it seems only fair to assume that many of the cultures of material from the nose and throat that were positive for hemolytic streptococci would likely contain the so-called scarlet fever strain, because the patients for whom the cultures were made were from the general population, and many of them were scarlet fever contacts. If the assumption just stated is correct, it seems evident that sporadic cases of scarlet fever would occur in a children's hospital, where not only are there a large number of susceptible contacts but at least 25 per cent of the patients and 15 per cent of the personnel have cultures of material from nose and throat positive for strains of hemolytic streptococci.

Of the 150 members of the personnel of the general hospital for whom cultures and Dick tests were made on March 4, 1934, 4 had positive cultures and positive Dick reactions and 17 had positive cultures and negative Dick reactions. Nineteen per cent of those with a positive culture gave a history of sinus disease, while only 11 per cent of those with negative cultures gave such a history. Cultures were positive for 13.3 per cent of the nurses and interns. In the group with positive cultures only 30 per cent had had their tonsils removed, while 58 per cent of those with negative cultures had had a tonsillectomy. A careful examination of the nose and throat was made at the time the material for culture was taken, that it might be determined whether rhinitis, reddening of the pharynx or a postnasal drip was present. One or more of these inflammatory changes were present in 57 per cent of those with positive cultures, but similar changes were present in 32 per cent of the group with negative cultures. A positive Dick reaction was present in 30 per cent of the whole group. When the nurses and interns were considered, it was found that 32 per cent of them were positive Dick reactors. The Dick reaction had been previously reported as negative for 5 of the positive reactors. Five of the positive Dick reactors gave a history of having scarlet fever, and for 3 others there was a history of immunization against scarlet fever one, four and six years previously, respectively. Twenty per cent of the whole group gave a history of having scarlet fever, the incidence being 5.5 per cent higher in nurses and interns.

Among the 388 members of the children's hospital personnel for whom cultures were made on Jan. 4, 1934, there were 213 nurses, interns and attending staff physicians. A positive culture and a positive

Dick reaction were observed for 2 of the personnel, while for 60 there were positive cultures and negative Dick reactions. A history of sinus disease was obtained from 21.5 per cent of those with positive cultures, the percentage being approximately the same as for the general hospital group; but in this survey 20 per cent of those with negative cultures also gave such a history. This would indicate the small influence of sinus disease in relation to positive cultures. Inflammatory changes in the nose or throat were present in 45 per cent of those with positive cultures and in 22 per cent of those with negative cultures, which is about the same incidence as in the general hospital group. The tonsils had been removed from 56 per cent of those with positive cultures and from 58 per cent of those with negative cultures. Of those with positive cultures only 58 per cent were nurses, interns and attending physicians, although they had a closer contact with patients than the rest of the personnel. In 30 or 8.5 per cent of the whole group the Dick reaction was positive, a proportion which contrasts with the incidence of 30 per cent in the general hospital group. A greater effort was made for immunization in the children's hospital group. Only 4.3 per cent of the nurses and physicians had a positive Dick reaction. A positive reaction was present in 4 nurses after immunization against scarlet fever and in 9 of the personnel with a history of having scarlet fever. Twenty-two per cent of the personnel gave a history of having the disease. Such a history was 5 per cent more frequent for the nurses and doctors than for the other employees. These figures compare closely with those of the general hospital group.

Cultures were positive for 44.5 per cent of the 124 children included in the hospital patient survey of January 1934. Of those children with positive cultures 24.6 per cent had had their tonsils and adenoids removed, and of those with negative cultures 15.2 per cent had had a similar operation. Inflammatory changes in the nose and throat were present in 30 per cent of the children with positive cultures as compared with an incidence of 20 per cent in those with negative cultures. There was a positive Dick reaction in 35.8 per cent of the whole group. Twenty-one, or 17 per cent, of the group gave a history of having scarlet fever, and in 5 of these the Dick reaction was positive.

In order to determine whether cultures of material from the nose or throat have a greater tendency to be positive for patients resident in the hospital than for patients after discharge from the hospital cultures were made again for two such groups. The interval between the first and the second culture varied from one month to one year. In selecting the 388 patients resident in the hospital during the entire interval between cultures, the results of the first culture were disregarded. When first tested, 19.6 per cent of these patients had positive cultures, and 17 per cent had positive second cultures. Of the 76 children who

originally had positive cultures 31.6 per cent again had positive cultures and 10.2 per cent of those who originally had negative cultures had positive ones.

Four hundred and eighty-nine patients for whom cultures were first made in the hospital had cultures made in the outpatient department some time after discharge. In this group there was a selection of patients with previously positive cultures and positive Dick reactions because we were also interested in the relation of the Dick reaction to carriers of hemolytic streptococci. At the time of the first culture, 33 per cent of this group had positive cultures, but at the time of the second culture only 14.5 per cent did. This is a lower percentage of positive cultures than for the hospital group. Of the 162 children with originally positive cultures, 20.4 per cent continued to have them, while only 11.6 per cent of those with originally negative cultures later had positive ones. The number of children with negative cultures who later had positive ones is the same for both groups, but 11 per cent more of the hospital patients again had positive cultures. This persistence of positive cultures for hospital patients may play a large part in the occurrence of sporadic cases of scarlet fever in the hospital as well as in the development of secondary infection in the home after discharge of a patient from a hospital for contagious diseases, as will be brought out later.

In an attempt to ascertain for how long hemolytic streptococci could be cultured from material from the noses and throats of patients and personnel, for 39 of the former and for 50 of the latter with positive cultures of 10 per cent or more cultures were repeatedly made at five day intervals. It is unfortunate that cultures of material from the nose and throat could not have been made for each member of this group until they became negative. In table 2, in the column denoting negative cultures, the figures opposite the interval represent the number of persons for whom the cultures became negative at that period. In the column denoting cultures still positive, the figures represent the number of persons whose cultures were still positive but for whom culturing had to be discontinued at that period because of such circumstances as illness, change of duty or discharge from the hospital. It would seem from the experience with this group that children with positive cultures continue to have positive cultures for a shorter period than adults with such cultures. In table 3 examples of the persistence of positive cultures are given for 2 members of the personnel and 2 patients. In the culture column each figure represents the number of colonies or the percentage of hemolysis of the plate for each of the cultures taken at five day intervals.

From July 1934 to March 1936 all new members of the personnel, including nurses and interns, who were about to be employed in the

children's hospital were required to have material taken from nose and throat cultured for hemolytic streptococci before going on duty. There were 574 new members, of whom 550 had negative cultures and 24, or 4.2 per cent, positive. Of the latter, 9 had cultures under 10 per

TABLE 2.—*Persistence of Positive Cultures*

Number of Five Day Intervals	Personnel		Patients	
	Number of Cultures Remaining Positive	Number of Cultures Becoming Negative	Number of Cultures Remaining Positive	Number of Cultures Becoming Negative
2	..	..	2	2
3	..	..	2	..
4	..	6	3	3
5	4	3	1	1
6	4	4	3	2
7	1	2	4	4
8	2	2	..	..
9	3	1	1	2
10	1	2	1	1
11	2	..	2	..
12	..	..	1	..
13	2	1	..	..
14	1	..	..	1
15	1	1	..	1
16	2	..	..	..
17	1	..	..	2
20	2	..	..	..
21	2	..	..	..

TABLE 3.—*Examples of Persistence of Positive Cultures*

	Age	Culture Reading in Percentage of Hemolysis		Dick Test	History of Scarlet Fever	Comment
		Throat	Nose			
Nurse	21	100–90–90 10–25–75 50–75–75 25–100	25–1 col.–neg. neg.–neg.–neg. neg.–neg.–neg. neg.–neg.	Neg.	No	Sinusitis; large ragged tonsils; mild injection of throat
Dietitian	28	100–100–10 3 col.–10–90 6 col.–50–90 10–10–neg. 75–25–90 100–100–100	All neg.	Neg.	No	Large tonsils; no injection of throat
Patient with empyema	7	25–50–10 10–neg.–10 neg.–10–neg.	100–neg.–10 neg.–10–neg. neg.–neg.–neg.	Neg.	No	No injection of throat
Patient with Pott's disease	6	50–75–90 90–4 col.–75 10–10–neg. 25–50–75 25–10–10 neg.–neg.	1 col.–neg.–90 75–10–1 col. 10–4 col.–75 8 col.–neg.–neg. 10–10–neg. neg.–neg.	Pos.	No	Throat inflamed

cent positive, 13 from 10 to 50 per cent and 2 from 50 to 100 per cent. This incidence of 4.2 per cent of positive cultures is much lower than the incidence of 12 to 17 per cent which was always present after these persons had been on duty in the hospital for a time. It seems highly probable that contact with sick children causes this marked increase of positive cultures for hemolytic streptococci.

We were also interested in the frequency of positive cultures of material from the noses and throats of the personnel when an infection of the upper respiratory tract was present. Cultures of material taken on the first or second day of illness were made for 630 of the personnel with such infections. There were 153, or 24.3 per cent, who had positive cultures. With such a high incidence of positive cultures when infections of the upper respiratory tract are present, the danger of continuing on duty or of returning to duty before complete subsidence of the infection should be given serious thought.

Cultures of material from the noses and throats were made of nurses before they went on duty in the small contagious disease unit of the hospital. Cultures were again made at the end of that service, which lasted from one to three months. Of 92 nurses that went on duty in the contagious disease unit, 14 per cent had positive cultures; this was the average percentage for the entire personnel. At the conclusion of the service 24 per cent had positive cultures, although only 75 per cent had had contact with patients with scarlet fever. Fifty per cent of the nurses who had positive cultures before beginning this service had positive cultures at the end of the service.

Conclusions.—The incidence of cultures of material from nose and throat which were positive for hemolytic streptococci was only moderately higher for the personnel of the children's hospital than for the personnel of a general hospital.

A high percentage of the patients of a children's hospital had positive cultures.

More children had positive cultures after residence in the hospital than when admitted to the hospital.

When cultures were made for identical groups of personnel and patients on successive days, the number of positive cultures was about the same for both days, but only 50 to 70 per cent of those with positive cultures had positive cultures for both days.

Cultures tended to be more persistently positive for adults than for children.

The incidence of positive cultures for the personnel of a children's hospital was greater during employment than before such employment.

Nurses on duty in a contagious disease unit had positive cultures more frequently than those on general duty.

2. RESULTS OF CULTURES FOR PATIENTS ADMITTED TO THE HOSPITAL

Material from the noses and throats for cultures of hemolytic streptococci was taken from 4,151 patients when they were admitted to the Children's Memorial Hospital during 1934 and 1935 and during the

first three months of 1936. The material was taken on the day of admission as far as was possible. Patients admitted for tonsillectomy and adenoidectomy were not included in this study except during a few months of 1934.

The percentage of positive cultures by months is given in table 4. In both years the latter half of the winter months and the spring months had the highest incidence of positive cultures. This follows rather closely the monthly frequency of scarlet fever in the Chicago area during this same period, as will be shown later. There was little difference in the total number of positive cultures for 1934 and for 1935, the percentages being 18.9 and 19.2, respectively. It was interesting to note the infrequency of positive cultures of material from the

TABLE 4.—*Results of Cultures of Material from the Noses and Throats of Patients About to Be Admitted to the Hospital*

Month	1934			1935			1936		
	Total No. of Patients	No. Pos.	Percentage Pos.	Total No. of Patients	No. Pos.	Percentage Pos.	Total No. of Patients	No. Pos.	Percentage Pos.
January	56	10	17.9	102	17	16.7	85	19	22.4
February	83	20	24.1	114	25	21.9	59	17	28.8
March	156	40	25.6	99	30	30.3	87	16	18.4
April	229	57	24.9	119	33	27.7	..	..	....
May	263	68	25.9	141	33	23.4	..	..	....
June	221	40	18.1	145	38	26.2	..	..	....
July	267	45	16.9	130	16	12.3	..	..	....
August	197	25	12.7	146	23	15.7	..	..	....
September	236	26	11.0	127	17	13.4	..	..	....
October	288	52	18.0	120	18	15.0	..	..	....
November	268	47	17.5	120	15	12.5	..	..	....
December	179	31	17.3	114	19	16.7	..	..	....
Total	2,443	461	18.9	1,477	284	19.2	231	52	22.5

Total number with cultures, 4,151. Positive cultures, 797 or 19.2%.

noses. Of the positive cultures made during 1934, those of material from the nose were positive in 1.5 per cent of cases, from both the nose and the throat in 2.6 per cent and from the throat alone in 14.7 per cent. For 1935 the figures were 1.5, 3.5 and 14.3 per cent, respectively. If these figures hold true for the general population, the importance of cultures for hemolytic streptococci of material from the nose is of little consequence.

The relation of a positive or a negative culture to the presence or absence of the tonsils and adenoids and its relation to the presence or absence of a pharyngeal infection in 3,270 patients for whom cultures were made on their admission to the hospital is given in table 5. A careful examination of the nose and throat of each patient was made at the time of admission. Although the number of patients that had had their tonsils and adenoids removed was small, the results for all the groups check closely. Of the patients with a pharyngeal infection,

there were 6 per cent more with positive cultures in the group that still had their tonsils and adenoids than in the group without tonsils and adenoids, while of the patients without pharyngeal infection there were only 3 per cent more with positive cultures in the group that still had their tonsils and adenoids than in the group without tonsils and adenoids.

However, when the patients that had had their tonsils and adenoids removed were grouped according to the presence or absence of a pharyngeal infection, it was found that the percentage of positive cultures was the same for both groups. When a similar comparison was made of the patients that still had their tonsils and adenoids, it was found that there was an increase of only 3 per cent in the positive cultures when a pharyngeal infection was present. It would seem, then, that while pharyngeal infections alone influence little the presence of hemo-

TABLE 5.—*Relation of Positive Cultures to Tonsillectomy and to Infections of the Upper Respiratory Tract in the Patient's Families*

	Tonsils Present			Tonsils Removed			History of Infection of Upper Respiratory Tract in Family: Yes			History of Infection of Upper Respiratory Tract in Family: No		
	Number Tested	Number Positive	Percentage Positive	Number Tested	Number Positive	Percentage Positive	Number Tested	Number Positive	Percentage Positive	Number Tested	Number Positive	Percentage Positive
Patients with infections of upper respiratory tract	1,002	230	23	157	26	17	319	80	25	846	184	22
Patients without infections of upper respiratory tract	1,845	375	20	266	46	17	251	48	19	1,902	353	19

lytic streptococci in the nose and throat, the added presence of tonsils and adenoids does seem definitely to influence the frequency of positive cultures.

Although a history of infections of the upper respiratory tract in the families of this class of patients tends to be highly unreliable, such data were collected. The parent of the patient was questioned as to whether any member of the family living in the home had or had had an infection of the upper respiratory tract during the previous eight weeks, a period which may be considered too long when contact infections are being considered. From 3,318 families fairly accurate information as to previous infections was obtained (table 5). The presence of an infection in the family had little influence on the percentage of positive cultures in the patient. But when the patient also had an infection of the upper respiratory tract, positive cultures were more frequent.

When the frequency of positive cultures for these groups of patients was compared according to age, it was found that there was little or no variation for each year of age from the fourth to the twelfth. From

an age under 1 year to the fourth year the frequency was slightly less than with the more advanced ages.

In order to determine whether the size of the family had an influence on the presence of a positive culture, 3,700 patients' families were grouped as to the number of members (table 6). Patients between birth and the age of 5 years were placed in one group and those between 5 and 12 years in another. In the group of young children 17 per cent had positive cultures, as compared with 22 per cent in the older, or school age, group. The size of the family from which the patient came had no influence on the percentage of positive cultures in either age group.

The general average of positive cultures for hemolytic streptococci on admission was 19.2 per cent, as compared with an average of 25 per cent for patients resident in the hospital, the proportions having

TABLE 6.—*Positive Cultures in Relation to Size of the Patients' Families*

Number of Members in Patient's Family	From Birth Through 5 Years			From 6 to 12 Years Inclusive		
	Total Number of Patients' Cultures	Number Positive	Percentage Positive	Total Number of Patients' Cultures	Number Positive	Percentage Positive
2	20	0	0	26	6	23
3	267	41	16	188	38	20
4	460	80	18	520	129	25
5	337	52	16	497	110	22
6	221	38	18	367	78	21
7	129	22	17	197	38	19
8	74	16	22	137	26	19
9	47	15	30	62	13	21
10	60	11	19	91	18	20
Totals.....	1,615	275	17	2,085	456	22

been established on several culture surveys. The increase of positive cultures for hospital patients was possibly due to the contact between patients with positive and those with negative cultures and to the fact that patients with infections were kept in the hospital for the longest periods. While 4.2 per cent of the personnel had positive cultures before employment, 14 per cent to 17 per cent had positive cultures after being on duty. Of those who had infections of the upper respiratory tract, 24.2 per cent had positive cultures at the same time. This increase did not take place in children when a pharyngeal infection was present. That positive cultures were frequent for children when no infection of the throat or nose was present was emphasized when patients admitted solely for tonsillectomy were studied. Of 832 such patients, supposedly with no infection of the nose and throat, twenty-four per cent had positive cultures of material from the nose and throat.

Conclusions.—For children the incidence of positive cultures for hemolytic streptococci of material from the nose and throat varied with seasons, but the yearly variation was slight.

For children about to be hospitalized, hemolytic streptococci were cultured from material from the nose alone for 1.5 per cent, from both the nose and the throat for 3 per cent and from the throat alone for 14.5 per cent.

Cultures positive for hemolytic streptococci were moderately more frequent for patients with tonsils and adenoids.

Pharyngeal infections in children did not seem to increase the incidence of positive cultures for hemolytic streptococci in material from the nose and throat.

Positive cultures of material from the nose and throat were no more frequent for patients from families with infections of the upper respiratory tract than in those from families without such infections.

The size of the family bore no relation to the incidence of positive cultures for the patient.

The frequency of positive cultures varied little with the age of the patient, except for a moderate decrease under the age of 5 years.

Children about to be admitted to the hospital had a lower incidence of positive cultures than patients resident in the hospital.

Positive cultures were more frequent for children than for adults.

3. THE DICK TEST

Dick tests were performed on all patients admitted to the Children's Memorial Hospital at the same time that cultures of material from the nose and throat for hemolytic streptococci were being taken. All the Dick tests were made and the results read by the same persons, in order that there might be as much uniformity as possible in testing and interpretation. Dick tests were made on approximately 5,000 children. Two groups of patients had a second Dick test some months after the initial test in order that information might be gained as to the influence of positive cultures on the changing of the Dick reaction.

The results of the Dick test on 3,710 patients are given in table 7. As has often been demonstrated, there was a gradual decrease in the number of positive reactors as the children became older. In this series the positive reactors decreased from 71 per cent in the 1 year age group to 28 per cent in the 12 year age group. Only 34 per cent of the infants under 1 year of age had a positive Dick reaction. As will be shown later, the Dick reaction during this age is extremely unstable, frequently changing from negative to positive. When the children that had had their tonsils removed were compared with the group in which such an operation had not been performed, it was found that in the whole age group 38 per cent of the former and 49 per cent of the latter had positive reactions. Although it is claimed that scarlet fever occurs much less frequently in children that have had a tonsillectomy, a posi-

tive Dick reaction was only 11 per cent less frequent in this group. This decreased frequency, then, could hardly be due to the higher number of susceptible members of this group as measured by the Dick test. Of 3,710 children admitted to the hospital, only 509, or 13.7 per cent, had had a tonsillectomy; if only those children over 4 years of age are considered, the figure is only 482, or 21.9 per cent. Positive cultures for hemolytic streptococci material from the nose and throat were only 3 per cent more frequent when no infection of the throat was present and 6 per cent more frequent when such an infection was present in children with tonsils and adenoids than in children who had had a tonsillectomy. In other words, aside from the 11 per cent fewer susceptible tonsillectomized children there were practically four times more

TABLE 7.—*Relation of Dick Reaction to Presence of Tonsils*

	Tonsils Out			Tonsils In			Both Groups		
Age, Yr.	Total Number Tested	Number Positive	Percentage Positive	Total Number Tested	Number Positive	Percentage Positive	Total Number Tested	Number Positive	Percentage Positive
Under 1	1	0	0	414	139	34	415	139	34
1	6	5	84	301	212	71	307	217	71
2	4	3	75	251	189	76	255	192	75
3	7	6	86	240	165	69	247	171	69
4	9	6	67	277	167	60	286	173	61
5	23	9	40	301	166	55	324	175	54
6	47	27	58	289	134	47	336	161	48
7	56	17	30	273	118	44	329	135	41
8	49	22	45	240	98	41	289	121	41
9	72	21	30	197	66	33	269	87	32
10	75	25	33	185	63	35	260	88	34
11	71	23	33	124	29	24	195	52	27
12	89	26	30	109	29	27	198	55	28
Totals..	509	190	38	3,201	1,575	49	3,710	1,765	48

children with tonsils and adenoids to contract scarlet fever. Removal of the tonsils and adenoids at an early age does not insure against the occurrence of scarlet fever.

In order that we might determine whether children that had positive hemolytic streptococcic cultures of material from the nose and throat were more likely to have a negative Dick reaction than children with negative cultures, 859 patients were given a second Dick test within a year of the first. Two separate groups of patients were retested. In one group the patients were resident in the hospital during the entire interval between tests. The second group, comprising 489 patients, were retested in the outpatient department some time after discharge from the hospital.

In table 8 it is seen that of the 71 per cent of the group who reacted positively to the first Dick test, 62 per cent still reacted positively to the second, 9 per cent now reacting negatively. About one fourth of those whose reactions became negative were under 1 year of

age. While 29 per cent of the patients had negative reactions when first tested, on the second test only 24 per cent of these continued to react negatively, and in 5 per cent the reaction became positive. About three fourths of those whose reactions became positive were under 1 year of age. The Dick reaction is extremely unstable in patients less than 1 year old. In 11 instances the Dick reaction changed from negative to positive in children over 2 years of age. It may be argued, and rightly so, that there was some error in technic which caused this variation in the Dick reaction. Owing to the experience of the person who performed the tests and to the care of the solutions, we feel that the technic was as good as or better than that used in the average physician's office. The error in technic, if there was an error, was of

TABLE 8.—*Changes in Dick Reaction Within One Year*

Age	Total No. of Patients	No. of Positive Reactors to First Test	Results of Second Test		No. of Negative Reactors to First Test	Results of Second Test	
			Positive	Negative		Positive	Negative
Under 6 mo.	69	15	12	3	54	27	27
6-12 mo.	55	39	30	9	16	3	13
12-18 mo.	38	29	28	1	9	..	9
18 mo.-2 yr.	75	53	45	8	22	1	21
2-3 yr.	70	60	55	5	10	2	8
3-4 yr.	74	65	55	10	9	..	9
4-5 yr.	83	69	60	9	14	3	11
5-6 yr.	73	58	50	8	16	2	14
6-7 yr.	82	57	53	4	25	1	24
7-8 yr.	59	50	45	5	9	1	8
8-9 yr.	59	41	34	7	18	..	18
9-10 yr.	61	37	34	3	24	..	24
10-13 yr.	60	37	30	7	23	1	22
Totals	859	610 71%	531 62%	79	249 29%	41	208 24%
Totals for all over 1 yr. of age	735	556 76%	489 67%	67	179 24%	11	168 23%

the same type as would occur in testing in one's office and would lead to the same false interpretation of the Dick reaction, with a consequently false sense of security.

Of the 610 children that had a positive Dick reaction on the first test, 181, or 30 per cent, also had a positive culture for hemolytic streptococci of material from the nose and throat. On the second Dick test, 18.2 per cent of these 181 children had negative reactions. Four hundred and twenty-nine of the children with a positive Dick reaction had a negative culture when first examined, and of these, 11.9 per cent had negative Dick reactions on the second test. In the presence of a positive culture of material from the throat, 6 per cent more of positive reactors became negative reactors than when a negative culture was present.

To determine whether the children of a large family were more apt to have a negative Dick reaction than those of a small family, the

children of 3,729 families were grouped according to the number of members in each family (table 9). There was definite decrease in the number of positive Dick reactors as there was increase in the size of the families. This was more marked in the children of school age. It seems likely that the lower incidence of positive Dick reactions in the larger family groups was due mostly to increase of contacts in the family, but consideration must also be given to the fact that there would be fewer older children in small families than in larger ones. This decrease of positive Dick reactions as families became larger does not seem to have been related to positive hemolytic streptococcic cultures of material from the nose and throat because, as previously shown, the size of the family bore no relation to the presence of a positive culture.

TABLE 9.—*Dick Reaction in Relation to Size of Patient's Family*

Number of Members in Patient's Family	From Birth Through 5 Years			From 6 to 12 Years			Both Groups	
	Total No. of Patients Tested	Number Positive	Percentage Positive	Total No. of Patients Tested	Number Positive	Percentage Positive	Number Positive	Percentage Positive
2	22	13	60	24	9	38	22	48
3	263	173	66	189	95	50	268	59
4	460	297	65	522	229	44	526	54
5	340	187	55	525	191	35	378	44
6	224	129	58	362	122	34	251	43
7	131	83	64	196	61	32	144	44
8	74	38	52	138	36	26	74	35
9	47	24	51	62	17	28	41	38
10 and over	59	29	50	91	19	20	49	32
Totals..	1,620	973	60	2,109	779	37		

A history of previous scarlet fever was obtained from 559 patients (table 10). At the time of their scarlet fever 329 children were quarantined in the home, and 167 were removed to a hospital for contagious diseases for care. Of those quarantined at home, 23 per cent now had a positive Dick reaction, as compared with 13 per cent of those quarantined in the hospital. This difference in the percentage of positive reactors between those in the hospital and those at home was most likely due to a more liberal diagnosis of scarlet fever in the home. Of children 3 years of age and younger with a history of scarlet fever, the Dick reaction was positive in 48 per cent of those quarantined at home and in 40 per cent of those quarantined in the hospital, as compared with 17 per cent and 11 per cent, respectively, of children between 3 and 12 years of age. This is a high incidence of failure of immunity after the disease, as measured by the Dick test. Such immunity is less apt to develop in children under 4 years of age.

At the time of the first survey of the personnel of the Children's Memorial Hospital, 30 of the 350 members of the personnel had posi-

tive Dick reactions. Eleven of these 30 had been reported as having previously had negative reactions and 9 as having had positive reactions. No Dick test had been made previously on 10 members of the personnel. Of the 30 persons with positive Dick reactions, half were nurses and interns, while the others were employees who had little or no contact with patients. Forty-six, or about one third, of the 150 members of the personnel of the general hospital were positive Dick reactors, of whom 29 were nurses and interns in close contact with patients. With such a high percentage of positive Dick reactors among the hospital personnel and patients, sporadic cases of scarlet fever are bound to occur because exposure is always taking place with the high constant level of hemolytic streptococcic carriers.

TABLE 10.—*Dick Reaction in Patients with a History of Scarlet Fever*

	Patients Quarantined* at Home				Patients Quarantined* in a Hospital			
Age, Yr.	No. of Patients	No. Positive	Percentage Positive	No. Negative	No. of Patients	No. Positive	Percentage Positive	No. Negative
Under 1	2	..	..	2	1	1	100	..
1	5	3	60	2	..	..	..	..
2	9	5	56	4	2	1	50	1
3	15	7	47	8	7	2	29	5
4	15	1	7	14	19	3	16	16
5	26	13	50	13	19	..	..	19
6	31	3	10	28	27	3	12	24
7	50	13	26	37	19	4	21	15
8	36	5	14	31	10	..	..	10
9	37	5	13	32	25	3	12	22
10	42	8	20	34	16	4	25	12
11	32	6	19	26	13	..	..	13
12	29	6	21	23	9	..	..	9
Totals	329	75	23	254	167	21	13	146

* Quarantine in home or hospital was not stated of 63 patients. Of these the Dick reaction was positive in 19, or 30 per cent.

Conclusions.—The reaction to the Dick test was extremely changeable during the first year of life.

Positive reactions were 11 per cent less frequent in children that had had a tonsillectomy.

The reaction changed from positive to negative in 6 per cent more children when a positive hemolytic streptococcic culture of material from the nose and throat was present than when a negative culture was present.

In a small number of children (1 per cent) over 2 years of age the reaction changed from negative to positive.

A negative reaction was more apt to be present in the children of larger families than in those of smaller families.

A positive reaction was present in from 13 to 23 per cent of children who gave a history of having scarlet fever. The figures were even higher for children under 3 years of age who had had scarlet fever.

Scarlet fever may well occur sporadically in hospital patients because of the high incidence of carriers of hemolytic streptococci and of positive Dick reactors in both the personnel and the patients.

4. SCARLET FEVER IN A CHILDREN'S HOSPITAL

During the latter part of 1933 the sporadic occurrence of scarlet fever in both the patients and the personnel of the Children's Memorial Hospital was of such frequency as to be of epidemic proportions. It was this frequency of the disease that led to the present study of scarlet fever, Dick reactions and cultures for hemolytic streptococci of material from the noses and throats of patients and personnel during 1934 and 1935.

Of the 82 cases in which a diagnosis of scarlet fever was made, in 76 the disease occurred in patients and in 6 in members of the personnel of the hospital. Four of the patients had surgical scarlet fever, with

Scarlet Fever Occurring in the Hospital

Period	No. of Cases	Incidence	
		Patients	Employees
Sept. 1933 to Jan. 1934	21	17	4
Jan. 1934 to Jan. 1935	23	22	1
Jan. 1935 to Jan. 1936	23	23	..
Jan. 1936 to June 1936	15	14	1

cultures of material from the nose and throat negative for hemolytic streptococci.

It was not always easy to decide whether scarlet fever was contracted before or after admission to the hospital. If the symptoms of the disease were not evident until seven or more days after admission, then one can assume that the infection was contracted in the hospital. But if symptoms appeared between the third and the seventh day after admission, the infection probably occurred before hospitalization, although there is a fair possibility that it may have occurred after entry. Each of these borderline decisions had to be made individually. It was felt that 59 of the 75 patients with scarlet fever contracted the disease in the hospital and that 17 had the disease or the infection at the time of admission. Of the 4 cases of surgical scarlet fever, the rash in 1 appeared within twenty-four hours after hospitalization and in the 3 others five, seven and ten days, respectively, after admission. In the latter 3 cases the patients were considered to have contracted the disease after admission, although the infection may have been present previously. Only 4 private patients had scarlet fever, 1 having the infection on admission and 3 contracting the disease after admission.

Material from the nose and throat for cultures for hemolytic streptococci was not taken from 31 patients and from 4 members of the hospital personnel before scarlet fever was contracted. In the remaining 47 cases, material for such cultures had been taken. Of 10 patients who we felt had the infection at the time of admission to the hospital, 9 had positive and 1 negative cultures. In the last case the scarlet fever rash developed three days after hospitalization, and the disease may have been contracted after admission, although there was no known contact. Material for cultures had been taken on admission from 31 patients who contracted the disease some time after hospitalization. Twenty-seven had negative cultures and only 4, or 13 per cent, had positive cultures, which is somewhat less than the average of all patients about to be admitted, 19 per cent of whom had positive cultures. Of 2 nurses who contracted scarlet fever, 1 had previously had a negative culture and the other a positive one shortly before the disease developed. The 4 patients with surgical scarlet fever were not included in the figures just cited, although all had negative cultures of material from the nose and throat. Material for culture had not been taken from the wounds until after the disease developed.

Dick tests were not made on 8 of the 17 patients who we felt had the infection when admitted, but 5 still had positive reactions and 3 negative ones. Of the 59 patients in whom scarlet fever developed some time after admission to the hospital, 22 were not given Dick tests, 35 had a positive reaction, and 2 had a reaction with a nodule that was read as negative. All 6 members of the personnel who contracted the disease had had a supposedly negative Dick reaction. All but 1 of the 6 tests were done by some other person before this survey was started.

It is interesting to see where and when scarlet fever developed in the hospital. It occurred sporadically throughout all the wards at various times. The hospital is divided into floor units, each unit being separate, with no communication between patients. The medical and general surgical units are made up of six bed and four bed open wards and a few wards with partial partitions. Patients are admitted to the wards without previous routine isolation. The units for patients with orthopedic, cardiac and nephritic disease and those for convalescent patients are made up of large open wards. The infants' unit has individual cubicles.

From September 1933 to May 1934 scarlet fever occurred in 27 hospital patients and in 4 members of the personnel. During this period no complete list was kept of all possible patient or personnel contacts of these patients, nor were cultures made for the contacts after exposure. In 6 patients the scarlet fever infection was undoubtedly present on admission. Of the 25 remaining cases, in which the infection took

place while the patients were in the hospital, in only 9 could any exposure to a patient with scarlet fever be traced. In these 9 cases the disease occurred in the various hospital units.

1. Two patients were admitted to the medical unit with scarlet fever on Nov. 11 and 16, 1933, respectively, and were put in immediate isolation. One of the nurses who was taking care of these patients manifested scarlet fever on November 26, and on November 29 another child in the same unit, who was exposed to the nurse, showed the disease.

2. In December 2 boys in the boys' ward and 3 girls in the girls' ward of the cardiac and nephritic unit manifested scarlet fever. The boys, in whom the disease developed on December 7 and 23, respectively, had no known contacts. The girls, in whom it developed on December 14, 20 and 27, had no known contact for the primary infection, but all were in contact with each other.

3. In the orthopedic unit a nurse had scarlet fever on December 23. On December 24 and 28, 2 girls in contact with each other and with the nurse and on December 28 a boy in contact with the nurse manifested the disease.

4. Scarlet fever developed in the convalescent unit on December 24 and 28 and on Jan. 2, 1934, in 3 girls in contact with each other but having no known contact with a primary infection.

None of the remaining 17 patients had known contact with scarlet fever. In these cases the disease occurred sporadically throughout the whole hospital, and although several patients may have had it in one unit, the interval and the failure of any history of contact made it impossible to find the source of the infection.

From May 1934 to May 1936 scarlet fever occurred in 46 patients and in 2 members of the hospital personnel. Eleven of these patients had scarlet fever when admitted, and immediate isolation was carried out. In only 4 of the remaining 35 patients was there any direct contact with other persons with scarlet fever. 1. In the medical unit a patient without any known contact showed the disease on April 19, 1935, and on April 22 a contact of this patient contracted the disease. 2. In November 1935 scarlet fever occurred in 4 patients in the surgical and private ward unit. Two of the patients were in a semiprivate, two bed ward. In the first case scarlet fever was diagnosed on November 20, with contact being known, and in the second on November 26. The 2 patients in the charity ward were in contact with each other from their admission on November 21. One child became ill with the disease on November 24 and the other on November 26. It was assumed that the first child already had the infection when admitted. This also may be true for the second patient, but there is a possibility that the infection may have occurred from contact with the first.

During the period from May 1934 to May 1936 an attempt was made to check every contact, whether patient or employee, of all patients with scarlet fever in the hospital. There were 245 patients that had some contact with 40 children in whom scarlet fever developed while they were in the hospital. Of these 245 patients, 89 had positive Dick reactions, 145 had negative ones and 11 were not tested on admission. Although 5 of the 89 children with positive Dick reactions did not contract scarlet fever from these known exposures, they did have the disease later, when there was no known exposure. Thirty-eight other children (12 with positive Dick reactions, 25 wiith negative reactions and 1 not given a Dick test) had been in known contact with patients with scarlet fever from one to four times without contracting the disease. The 4 cases mentioned in the preceding paragraph are the only cases of scarlet fever which occurred within seven days of contact with a patient who had scarlet fever in the hospital, although during this period the disease developed in 37 patients sufficiently long after admission to make it seem that infection took place in the hospital. Of the 245 contacts, 48 had positive cultures of material taken on admission, 145 had negative cultures and for 12 no cultures had been made.

All patients and personnel in contact with 23 patients who had scarlet fever had positive cultures for hemolytic streptococci of material taken from the nose and throat at the time of contact. For the employees exposed to an additional 5 patients cultures were also made. From 129 patients in this group material for culture was taken at the time of exposure. On admission 25, or 19 per cent (which is the general average), had positive cultures, but 47, or 36 per cent, of this group had positive cultures of material taken at the time of contact with a patient who had scarlet fever. Twenty-nine of the 104 patients who had negative cultures on admission had positive cultures after exposure, and 18 of the 25 patients who originally had positive cultures again had positive ones after exposure.

During this same period for 512 members of the hospital personnel that had been in contact with patients with scarlet fever cultures were made at the time of such contact. Sixty-seven, or 13 per cent, had positive cultures. Twelve per cent of this group had positive cultures of material taken from a few weeks to a month previously. When the results of cultures of material taken at the time of exposure were compared with those of material taken previously, it was found that 20 of the 65 persons who originally had positive cultures again had positive ones and that 47 of the 444 who originally had negative cultures now had positive ones. This percentage of positive cultures is about the general average found during various hospital surveys.

After January, 1934, when any member of the personnel had a positive culture of 10 per cent or more, he was required to wear a mask or,

if the work involved contact with patients, was taken off duty. As to the yearly incidence of scarlet fever in the hospital, it can be seen that there was marked reduction in the number of cases after this study was started, in 1934. This may have been brought about by the isolation of children with cultures over 10 per cent positive and by requiring the hospital employees with positive cultures either to be off patient duty or to wear masks. A negative Dick reaction was required of all of the personnel who were in contact with patients. With this routine only 1 nurse and 1 employee in the diet kitchen (the latter having no contact with patients) contracted scarlet fever in two and one-half years. It is interesting to note that during the two years when the number of cases of scarlet fever was decreasing the disease was increasing in Chicago, with 9,453 cases in 1934 and 15,989 in 1935.

The elimination of scarlet fever in a hospital with open wards is extremely difficult because of the contact between children that are admitted during the incubation period of the disease and because of the high incidence of positive hemolytic streptococcic cultures of material from the noses and throats for both the patients and the personnel. In only 13 of the 65 cases in which we felt that the disease developed after hospitalization were we able to trace contact with other patients. In the other cases the disease developed sporadically throughout the hospital, and always the percentage of positive cultures for all patient contacts was markedly increased. In order that scarlet fever might be controlled in hospital patients, all patients would have to have negative Dick reactions or negative cultures, which is not possible, or to be in isolation. Even the latter method would not be entirely effective.

Material from the noses and throats of approximately 4,151 children was taken for culture on their admission to the Children's Memorial Hospital. The family names of these patients were checked against the records of the Department of Health to find out if scarlet fever had developed in any family after discharge of the patient from the hospital. In the families of 2 children (both of whom had negative cultures in the hospital) scarlet fever developed in 1 case within one week after the patient returned home. In 2 instances the discharged patient manifested the disease within one week after returning home. In 7 families scarlet fever occurred in 1 instance during the second week after a patient returned home (6 patients had had negative and 1 a positive culture in the hospital). During the third and fourth week after discharge scarlet fever developed in patients' families in only 3 more instances. Thereafter scarlet fever occurred in the families of discharged patients with an average of 5 cases per month. Scarlet fever was two and one-half times more common in the home during the first two weeks after the return of our discharged patients than it was during

the following months. There was no relation of positive cultures in the hospital to the frequency of occurrence of these cases.

Conclusions.—Sporadic cases of scarlet fever were of frequent occurrence in a children's hospital.

The number of such cases was thought to have been reduced by isolation of patients with positive cultures and by removal from patient duty of nurses with positive cultures.

Some sporadic cases of scarlet fever were bound to develop because of the high incidence of positive cultures in both personnel and patients and because of the high percentage of patients with positive Dick reactions.

In comparatively few of the cases of scarlet fever could exposure be traced to other patients with the disease in the hospital.

For patients with known exposure to scarlet fever there was a definite increase in the frequency of positive cultures.

The ideal way to control scarlet fever in a children's hospital would be to require negative Dick reactions of both personnel and patients.

5. SCARLET FEVER IN CHICAGO

The records of the Chicago Department of Health concerning scarlet fever occurring in 1934 and 1935 were studied. Information was obtained as to age and seasonal incidence; the number of days of illness before the disease was reported; the time of occurrence of secondary infection before, during and after establishment of quarantine at home or in the hospital; the number of cases of secondary infection occurring after release from quarantine in the hospital and in the home, and the number of cases per family in relation to the size of the family. This information was then correlated with the age incidence of positive Dick reactions and the age and the seasonal incidence of positive hemolytic streptococcic cultures of material from the nose and throat.

During 1934 and from January to May of 1935 the period of quarantine was three weeks, while after May 1935 it was raised to four weeks. This difference in the period was taken cognizance of when the number of cases of secondary infection was estimated. In 1934, 9,453 cases of scarlet fever were reported in the city. In 1935 the number was 15,989, an extremely high incidence. The number decreased to 7,918 in 1936.

In table 11 the monthly distribution of the disease is given for each of the three years. Although there were a rising frequency of scarlet fever during 1934 and through the first half of 1935 and a decreasing frequency during the latter half of 1935 and through 1936, the monthly percentage of cases compared closely from year to year. The winter and spring months consistently showed the highest incidence of the disease.

With the establishment of the four week quarantine in 1935 there was a marked decrease in the frequency of the disease, so that the figures for 1936 compared closely with those for 1934, when the three week quarantine was being used. It may be questioned whether the lengthening of the quarantine alone brought about this decrease in the frequency of the disease or whether the epidemic itself was receding owing to natural causes. When the seasonal incidence of positive cultures is compared with that of scarlet fever, it is found that they follow closely the same curve.

The distribution of cases of scarlet fever according to the age of the patients is given in table 12. There was a steady increase in fre-

TABLE 11.—*Monthly Distribution of Cases of Scarlet Fever*

	3 Week Quarantine				4 Week Quarantine					
	1934		Jan. to May 1935		May to Dec. 1935		1936		Percentage of Pos. Cultures 1934	Percentage of Pos. Cultures 1935
Month	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage		
Jan.	915	9.7	1,532	9.6	...	...	690	12.5	17.9	16.7
Feb.	1,059	11.2	2,176	13.6	...	...	976	12.3	24.1	21.9
March	1,193	12.6	2,842	17.8	...	...	1,237	15.6	25.6	30.3
April	1,094	11.6	2,930	18.3	...	...	961	12.0	24.9	27.7
May	1,119	11.8	.....	....	2,630	16.4	806	10.2	25.9	29.4
June	661	7.0	.....	....	1,480	9.3	613	7.7	18.1	26.2
July	228	2.4	.....	....	341	2.1	285	3.6	16.9	12.3
Aug.	160	1.7	.....	....	166	1.0	162	2.0	12.7	15.7
Sept.	318	3.4	.....	....	209	1.3	154	1.9	11.0	13.4
Oct.	577	6.1	.....	....	457	2.9	319	4.0	18.0	15.0
Nov.	923	9.8	.....	....	720	4.5	594	7.5	17.5	12.5
Dec.	1,193	12.6	.....	....	505	3.2	821	10.4	17.3	16.7
	13*				1*					
Totals	9,453		9,480†		6,509†		7,918			

* Incomplete information.
† The total number of cases for 1935 was 15,989.

quency through the sixth year, after which there was a steady decrease each year. Although the number of susceptible persons, as measured by the Dick test, decreased steadily with age, the age incidence was not the same as for scarlet fever. This difference was undoubtedly due to the comparatively small number of contacts for young children. In the period after the sixth year, when the opportunities for exposure are about equal for all persons, the incidence of the disease decreased approximately equally with the decrease in the number of susceptible persons. There was a more marked relationship according to age between the frequency of positive hemolytic streptococcic cultures of material from the nose and throat and the incidence of scarlet fever. Both reached their highest frequency between the sixth and the seventh year of age, although the curve for positive cultures is much flatter than that for scarlet fever.

Information was obtained as to number of days the patient had been ill before the case was reported to the department of health as one of scarlet fever. These figures (table 13) include cases of both primary and

TABLE 12.—*Frequency of Scarlet Fever, Positive Dick Reactions and Positive Cultures in Various Age Groups for 1934 and 1935*

Age, Yr.	Scarlet Fever		Positive Dick Reaction, Percentage†	Positive Cultures, Percentage†
	No. of Cases	Percentage		
Under 1	80	0.3	34	11.2
1	361	1.4	71	14.5
2	1,100	4.3	75	20.9
3	1,515	6.0	69	16.7
4	1,868	7.3	61	24.4
5	2,293	9.0	54	23.5
6	3,264	12.9	48	24.7
7	2,961	11.6	41	26.3
8	2,400	9.5	41	19.0
9	1,790	7.0	32	23.8
10	1,507	5.9	34	32.4
11	1,128	4.4	27	20.1
12	917*	3.6	28	17.9
13-16	1,715	6.7	..	....
17-20	575	2.3	..	....
21-30	1,232	4.8	..	....
31-45	661	2.6	..	....
Over 45	61	0.2	..	....
	6*			
Total	25,442			

* Incomplete information.
† Results of culture and of Dick tests for 3,300 children about to be admitted to the Children's Memorial Hospital.

TABLE 13.—*Number of Days of Illness Before Cases of Scarlet Fever Were Reported to the Department of Health*

Number of Days of Illness	Patients	
	Number	Percentage
1	732	2.9
2	3,655	14.4
3	6,140	24.1
4	5,158	20.3
5	3,377	13.3
6	1,655	6.5
7	1,110	4.4
8	439	1.7
9	205	0.8
10	354	1.4
11-14	802	3.2
15-21	854	3.4
Over 22	633	2.5
*	328	1.3
Total	25,442	

* Information incomplete.

secondary infection. They are similar for 1934 and 1935. About three fourths of the cases were reported from the second to the fifth day of illness, 25 per cent being reported on the third day. From the dates on the records this meant in the great majority of cases that the physician was called on that day. Because of this delay the other members of the

family usually had a corresponding number of days of exposure before a diagnosis was made and quarantine was established.

The occurrence of secondary scarlet fever in the family was of special interest. In all cases in which scarlet fever developed in the

TABLE 14.—*Time of Onset of Secondary Infection With Scarlet Fever After Exposure*

Group 1: Exposure Before Quarantine Was Established

No. of days	1	2	3	4	5	6	7	8	9	10	Over 10	Total	Total No. of Reported Cases
No. of cases	212	266	240	276	201	219	228	178	98	114	347	2,379	23,056*
Percentage of cases	8.9	11.2	10.1	11.6	8.4	9.2	9.6	7.5	4.1	4.8	14.5	10.3	

Group 2: Exposure During Quarantine at Home

Three week quarantine, 1934	No. of Weeks									Total No. of Patients Quarantined at Home
	2d	3d	4th	5th	6th	7th	8th	After 8th	Total†	
No. of cases	98	48	26	31	16	14	4	26	237	5,799
Percentage of cases	37.2	18.3	9.9	11.8	6.1	5.3	1.5	9.9	4.1	
Three week quarantine, Jan. to May, 1935										
No. of cases	139	70	31	30	14	15	10	12	309	7,722
Percentage of cases	44.9	22.7	10.1	10.0	4.5	4.9	3.1	3.7	4.0	
Four week quarantine, May to Dec. 1935										
No. of cases	50	30	18	32	20	11	5	18	166	4,742
Percentage of cases	30.1	18.0	10.8	19.3	12.0	6.6	3.0	9.8	3.5	

Group 3: Exposure During Quarantine in the Hospital

1934									Total†	Total No. of Patients Quarantined in Hospital
No. of cases	25	15	60	74	39	17	12	36	242	3,439
Percentage of cases	10.3	6.2	24.8	30.6	16.1	7.4	5.0	13.0	7.0	
Jan. to May 1935										
No. of cases	12	16	35	20	16	13	6	9	118	1,869
Percentage of cases	10.2	13.4	29.7	17.0	13.4	11.0	5.0	7.1	6.5	
May to Dec. 1935										
No. of cases	4	13	9	22	29	10	6	22	93	1,584
Percentage of cases	4.3	14.0	9.7	23.7	31.0	10.8	6.5	18.1	5.9	

* 1,843 cases of 2 or more patients in one family with the same date of onset not included.
† Cases of scarlet fever which occurred after the eighth week not included in totals.

family within eight weeks of the onset of the primary infection, the disease was considered as secondary. These cases of secondary infection have been divided into the groups to be described, according to the time of onset in relation to the cases of primary infection. In group 1 (table 14) were placed all those cases in which secondary infection

developed before quarantine was established as well as those in which the disease developed within seven days after quarantine was supposed to have been established. The seven day limit was taken arbitrarily because it seems to be the consensus that scarlet fever, if it is to develop, will present symptoms by the seventh day after exposure. The establishment of quarantine in the home or the removal of the patient with primary involvement to a hospital for contagious diseases would not affect the classification of cases of secondary infection in this group, because exposure to the disease had already taken place. In table 14 all the cases of secondary infection in group 1 were listed according to the day of onset of the disease as reckoned from the first possible day of exposure to the primary infection. The figures for the years 1934 and 1935 were combined in the table because the length of the quarantine would have no effect on this group. The percentages for the two years are so similar that comparison gives no added information. In the majority of cases of secondary infection the disease had developed by the eighth day after the first possible exposure, and the figures for each day between the second and the eighth do not show a wide variation. There was no correspondence between the day of the onset of the secondary involvement and the number of days of illness of the primary infection. This undoubtedly was due to irregular exposure in the cases of secondary infection. Moreover, the day of onset of the secondary infection may have been harder to fix because often more than one member of the family had the disease when the physician was called. There also may have been a tendency to date the onset of illness as close to the onset in another case as possible. Scarlet fever occurring in patients resident in hospitals or other institutions were not included in the groups.

In 1934 there were 1,001 cases of secondary scarlet fever, as classified in group 1. This is 11.7 per cent of the 9,453 cases occurring in 1934, excluding 209 cases of patients in institutions, including hospitals, and 650 cases in which the same day of onset was given for two or more members of the same family, so that cases of primary and of secondary involvement could not be differentiated. In these 650 cases the disease occurred in 295 families. If it is assumed that in each family there was 1 case of primary infection, then in the remaining 355 cases the infection can be considered as secondary. When these 355 cases are added to the 1,001, there is a total of 1,356, or 14.8 per cent, cases of secondary infection in group 1 in 1934. In 1935 there were 1,378 cases of secondary infection included in group 1. This is 9.5 per cent of the 15,989 cases of scarlet fever reported that year, excluding 334 cases of patients in hospitals and other institutions and 1,193 cases in which the same day of onset was given for two or more members of a family. In these 1,193

cases the disease occurred in 544 families. If it is assumed that in 544 cases the condition was primary, 649 cases would be added to the 1,378, making 2,027, or 13 per cent, cases of secondary involvement in group 1 in 1935. This compares with 14.8 per cent in 1934.

Included in group 2 (table 14) are all the cases of secondary scarlet fever that occurred in the family after the first week of home quarantine of the patient with primary infection. Only those cases in which the disease developed after the first week of quarantine were included in this group, because in those cases in which secondary infection occurred during the first seven days the patient might reasonably have become infected from exposure before quarantine was established. There was a three week quarantine during 1934 and from January to May of 1935 and a four week period from May to December 1935. During both years and for both periods of quarantine a large proportion of the cases of secondary infection occurred during the second week of quarantine. Several reasons can be given for this. It may be that quarantine was actually established not on the day the disease was reported but one or two days later. This would necessarily be true when the report to the department of health was made by mail. Quarantine may not have been adequately kept by the family. In some cases secondary infection may have a longer period of incubation than seven days. The percentage of cases of secondary infection decreased gradually from week to week, with a sharp drop after the fifth week in the group with the three week quarantine and after the sixth week in that with the four week quarantine. This interval of one week was undoubtedly due to delay in exposure during the first week after release from quarantine. Moreover, the quarantine would be lengthened if there were any complications. To account for the many cases of secondary infection which occurred during quarantine at home there must have been considerable exposure to the patient with scarlet fever, or to such possible carriers of the infecting organisms as the mother, who is usually the one to take care of the patient. It seems that most of the susceptible persons became infected during the early weeks of quarantine, which would account for the fact that there was no appreciable rise in cases of secondary infection the week after quarantine was discontinued. That these are plausible reasons becomes more evident when the figures for quarantine at home are compared with those of quarantine in the hospitals. It is to be noted that the incidences of 4.1 and 4 per cent of cases in group 2 in which secondary infection developed during the three week quarantine were only slightly higher than the 3.5 per cent incidence of the four week period. The age incidence in the cases of secondary infection in group 2 was about the same as in group 1. There was little difference in the two groups in this respect, the disease in the largest number of cases

occurring from the third through the eighth year of age. From these figures it seems that home quarantine is inadequate for the control of scarlet fever in families.

Included in group 3, table 14, are all those cases in which secondary scarlet fever developed in members of the family in the home after the patient with the primary infection had been removed to a hospital for contagious diseases and after his release from the hospital on termination of the quarantine. Only cases in which secondary infection developed after the first week were included in group 3, because during the first week the exposure may have occurred before the patient with the primary infection was removed from the home. The cases in which secondary infection developed during the three week quarantine of 1934 and 1935 and during the four week period of 1935 are given separately. In all three periods from 4 to 10 per cent of the patients with secondary infection manifested the disease from seven to fourteen days after removal of the patient with the primary infection to the hospital. In some the incubation period may have been longer than seven days. In many instances the patient with the primary infection was not removed to the hospital on the day the case was reported but one or more days later. There would then be the same possibility of exposure as in group 2. During the three week quarantine, in from 6 to 14 per cent of the cases of secondary infection the disease developed during the third week after removal of the patient with the primary infection. In 10 per cent of the cases the infection developed during the fourth week of the four week quarantine. As an explanation for the frequency of cases of secondary infection which developed so long after the removal of the patient with the primary infection, several factors must be considered. A person in close contact with the patient who has a primary infection, such as the mother, may become a carrier of hemolytic streptococci and transmit the infection to other members of the family. It was often extremely difficult to ascertain from the records whether a patient with secondary infection had been exposed only to the patient with the primary infection or to other patients in the family who had secondary infections. In addition, often 2 or more patients in a family apparently with secondary infections had onsets on the same day but with such an interval between that one patient may have contracted the disease as a result of exposure to the other. This would have considerable bearing on the figures as given in table 14, but from the available material no further information could be obtained. During the fourth week after onset in 1934 and from January to May 1935 (three week quarantine) the majority of the patients with primary infection were being discharged from the hospital to the home. This resulted in a large number of cases of secondary infection in the families during the fourth and the fifth week. This same situation

developed just one week later during the latter part of 1935, when the four week quarantine was in force. From this it would seem that the length of the quarantine in itself is not sufficient to control the development of secondary infection.

When the patient with the primary infection was quarantined at home, there was an incidence of 4.1 and of 3.5 per cent of cases of secondary infection, according to the length of the quarantine, as compared with an incidence of 7 and 5.9 per cent of cases of secondary infection which developed when the patient with the primary infection was quarantined in a hospital for contagious diseases. Because of this higher percentage of cases of secondary infection contracted from patients quarantined in a hospital, it would seem that carriers of the infecting hemolytic streptococcus are more frequent among hospital-quarantined than among home-quarantined patients with primary infection. The presence of complications should not be an influence, because patients are not supposed to be released until the infection has subsided or negative cultures have been obtained. A study comparing the results of culture at the termination of quarantine in the home and in the hospital would be of value. Hoyne and Bailey [1] have reported on the number of cases of secondary scarlet fever developing after discharge of patients with scarlet fever from a hospital for contagious diseases. They included only those cases in which secondary infection developed after the discharged vector had returned home. The incidence of such cases varied between 3.3 and 11.8 per cent, depending on quarantine regulations.

That the decrease in cases of secondary infection was not entirely due to the lengthening of the quarantine seems evident because from January to May 1935 there were fewer cases than in 1934, when the same three week period was in force. There was, though, a further decrease when the four week period was in effect. This decrease occurred from 1934 to 1935, when scarlet fever was increasing in the city. It is also interesting to note in how few cases scarlet fever occurred in families nine weeks or more after the primary infection. It almost seems as if few susceptible persons were left to contract the disease.

The number of cases of scarlet fever that occurred in families of different sizes is given in table 15. Cases in which the disease occurred in families of only 1 member and those in which it occurred in hospitals or other institutions were not included. In 7,304 families in 1934 there were 9,179 cases of scarlet fever, an average of 1.26 per family. During the similar quarantine in 1935, when scarlet fever was increasing at a rapid rate, 9,616 cases occurred in 7,792 families, a rate of 1.23 cases

1. Hoyne, A. L., and Bailey, J. H.: The Secondary Case of Scarlet Fever, J. A. M. A. **103**:1051 (Oct. 6) 1934.

per family. During the four week quarantine in 1935 there were 4,959 cases in 4,065 families, or 1.22 per family. The length of the quarantine had little or no effect on the number of cases per family. This is partly due no doubt to the fact that in the largest number of cases secondary infection develops from exposure which occurred before quarantine was established. Although scarlet fever occurred only once in 82 to 84 per cent of the families, in about 1.5 per cent of the families it occurred four or more times.

Excluding 209 cases in which the disease occurred in hospitals and other institutions, there were 9,244 cases of scarlet fever in 1934, of which 1,835, or 20 per cent, can be considered as cases of secondary

TABLE 15.—*Number of Cases of Scarlet Fever per Family*

Number in Family	Number of Cases							
	1	2	3	4	5	6	Over 7	Total
2	606	5	...	..	..	..	..	611
3	3,577	143	9	..	..	..	..	3,729
4	4,065	827	59	4	..	..	..	4,955
5	3,595	660	203	18	4	..	..	4,480
6	2,051	436	165	56	10	..	..	2,718
7	995	217	80	51	12	3	..	1,358
8	500	89	59	20	8	4	..	680
9	213	42	20	19	7	2	2	305
10	124	25	24	10	3	3	..	189
Over 10	80	27	11	7	3	4	4	136
Total	15,806	2,471	630	185	47	16	6	19,161
Percentage, 1934	81.7	13.2	3.5	1.1	0.3			
Percentage, Jan. to May 1935	82.4	12.7	3.2	0.9	0.3			
Percentage, May to Dec. 1935	83.8	12.6	3.1	0.7				

infection. In 1935, excluding 334 cases of the disease in institutions, there were 15,655 cases of scarlet fever, of which 2,713, or 17.3 per cent, can be considered as cases of secondary infection. In about 74 per cent of all the cases of secondary involvement the disease was due to exposure before quarantine was established. In the other 26 per cent the condition developed supposedly because of exposure after quarantine was established or because of exposure to vectors released from quarantine. In 1934 11 per cent and in 1935 5.8 per cent of all traceable secondary infection was due to exposure to vectors released from a hospital for contagious diseases. Such frequency of secondary involvement speaks against the present methods of quarantine.

Conclusions.—Changing from a three week to a four week quarantine did not control the development of secondary scarlet fever. It is questionable whether this change brought about the decreasing frequency of the disease during the period studied.

The seasonal incidence of scarlet fever was similar to, though fluctuating more widely than, the seasonal incidence of cultures positive for hemolytic streptococci.

Of the total cases of scarlet fever in 1934 and 1935, in 20 and in 17.3 per cent, respectively, the infection could be considered as secondary.

The age curve for scarlet fever bore no relation to the age curve for positive Dick reactions unil after the sixth year of life.

The length of the quarantine had little effect on the incidence of secondary infection.

In approximately 74 per cent of the cases of secondary infection the condition developed from exposure before quarantine was established.

From the number of cases in which secondary infection occurred during quarantine at home, it was evident that adequate quarantine is not enforced.

There was a high incidence of cases in which secondary infection was contracted from vectors who were released from the hospital for contagious diseases.

During the period studied there was an average of 1.25 cases of scarlet fever per family in which the disease occurred.

The ideal way to control scarlet fever would seem to be immunization of susceptible persons by some method.

6. RÉSUMÉ

Each of the preceding five sections of this paper deals with some phase of scarlet fever. This résumé is presented to see what it all means when the conclusions are applied to the spread and control of scarlet fever. By the term scarlet fever is meant the disease as it is commonly known, i. e., with the characteristic scarlet throat, the well known tongue signs and the toxic scarlet rash followed by peeling. If the rash was not observed during hospitalization, then the diagnosis was established by the infection of the throat and the positive culture, the tongue signs and the peeling typical as to time and character. Although it is realized that with pharyngeal infections (cultures positive for hemolytic streptococci) it is difficult to decide whether a diagnosis of scarlet fever is justified, such a diagnosis was made only if a rash or peeling was also present. This may be considered arbitrary, but a definite line had to be drawn for the purposes of this study.

In the preceding sections cultures positive for hemolytic streptococci and scarlet fever are spoken of as if one invariably followed the other. Available evidence indicates that the hemolytic streptococcus is the infecting organism of scarlet fever, but it is evident that not all strains of the hemolytic streptococcus produce the disease. Cultures for hemolytic streptococci are usually made on blood agar plates. By this simple

method the so-called scarlet fever strain cannot be differentiated from other strains, such as those claimed to be the cause of septic sore throat and erysipelas (assuming, of course, that these diseases are the result of infection with specific strains of the hemolytic streptococcus). Consequently, with blood agar culture one knows only whether or not hemolytic streptococci are present. It must be assumed, then, that any positive culture may contain a strain capable of causing scarlet fever. This holds true even when possible scarlet fever contacts are being considered as carriers of the infecting organisms. That a pharyngeal infection in children has little influence on the presence or absence of a positive culture was amply demonstrated in this study. It would be interesting to know just what strains of the hemolytic streptococcus are present in persons with normal-appearing throats, in those with infections of the throat and in those that are scarlet fever contacts. In this study we had to consider all persons with positive cultures as possible carriers of the scarlet fever strain of the hemolytic streptococcus. Dr. Ruth Tunnicliff made some culture studies on chocolate agar with 66 strains of the hemolytic streptococcus isolated in this study. At the time of writing Dr. Gladys Dick is doing some cutaneous tests with toxin from the same group of organisms. Both of these investigations will be reported later.

Seasonal incidence of positive cultures follows fairly closely that of scarlet fever, which indicates more than a casual relation between the two. Positive cultures were present for 19 per cent of the children to be admitted to the hospital, and approximately 25 per cent had positive cultures after residence in the hospital. But of that group of patients that had direct or possible exposure to a patient with scarlet fever which developed in the same ward, 36 per cent had positive cultures. In addition, at a time when many sporadic cases of scarlet fever occurred in the hospital, 44 per cent of the patients then resident had positive cultures.

That patients with positive cultures are of importance in the transmission of scarlet fever is further brought out by the fact that in only 13 of 65 cases of scarlet fever that developed in the Children's Memorial Hospital could the infection be traced to direct or possible contact with a patient who had scarlet fever. Unless some simple method of differentiating or identifying the various strains of the hemolytic streptococcus is made available, all persons with positive cultures will have to be considered as possible carriers of the organism which produces scarlet fever. This gives rise to a complex problem because of the following factors: According to the season of the year, 12 to 30 per cent of children will have positive cultures of material from the nose or throat, the frequency being considerably higher for patients resident in hospitals.

Positive cultures were nearly as often present for children with a normal-appearing throat as for those with a definite pharyngeal infection. When material for cultures was taken on successive days from the same group of children, only 30 to 50 per cent of the positive cultures were found with material taken from the same person on successive days. The frequency of positive cultures remained approximately the same for the years 1934 and 1935, although there were 60 per cent more cases of scarlet fever during 1935.

The percentage of positive reactors to the Dick test remained constant for both 1934 and 1935. This can be interpreted as meaning that a large number of susceptible persons escape the disease, even though the frequency of occurrence is of epidemic proportions. Here the epidemiology is different from the mode of operation of such contagious diseases as measles and chickenpox, which comparatively few susceptible persons escape when an epidemic is present.

That the information received from the Dick reaction is not always accurate seems evident from the fact that in 8 cases scarlet fever occurred in persons in whom the Dick reaction had been interpreted as negative. Two of these were patients, and 6 were hospital employees. Several hundred patients had rechecks of their Dick tests during the subsequent year, and in 1 per cent the reaction changed from negative to positive. It is true that while an error in technic would account for the negative reactions, the tests were all done with solutions of toxin that gave both negative and positive reactions. Positive Dick reactions were obtained in 16 of the hospital personnel, all of whom gave a history of negative reactions. As most of the nurses were affiliates from other institutions, only 1 of these 16 had previously been tested by us. Any technic that requires more than ordinary care is bound to lead to errors, and the possibility of error should always be given the utmost consideration.

Scarlet fever differs from most contagious diseases in that immunity, as measured by the Dick test, frequently does not develop after recovery from an attack of the disease. A Dick test was performed on 496 children who gave a history of having scarlet fever from one to five years previously. Twenty-three per cent of those quarantined at home and 13 per cent of those quarantined in a hospital for contagious diseases still had positive Dick reactions. This failure of immunity response as measured by the Dick test was influenced by the age of the patient. Second attacks of scarlet fever are not uncommon. It is possible that this failure of immunity after recovery from the disease may explain the occurrence of positive reactions following negative ones. Because of this failure of immunity from the disease itself one might well question the advisability of immunization against scarlet fever in young children.

Immunity to the hemolytic streptococcic diseases is evidently not as assured as is immunity to the other contagious diseases.

In gathering the material from the records of the Chicago department of health we designated as primary scarlet fever the first infection in the home and as secondary any subsequent infection in that home which occurred within seven days of the last possible contact. This should serve in a rough way as a measure of the contagiousness of the disease as well as of the infectivity of the infecting organism in relation to production of the disease. Of the total number of cases of scarlet fever reported in Chicago in 1934, in 20 per cent the infection was considered as secondary and directly traceable to a primary infection. In 1935, although the total number of cases reported was 60 per cent greater than in 1934, in only 17.3 per cent was the disease considered as secondary. The increase in scarlet fever which occurred cannot, then, be attributed to traceable secondary infection in the home. Whether these same averages would apply to schools or other gathering places cannot be stated. When the cases of secondary infection are considered, one gets the impression that practically all persons in the family who contract the disease do so within eight weeks after the primary infection occurred. In few cases did additional infection occur in an infected family within the following year. From this one is lead to believe that the infectivity of the organism in relation to the contagiousness of the disease does not change much from year to year.

In approximately 74 per cent of all the cases of secondary involvement the disease developed from exposure to the primary infection before quarantine was established. In most instances the patient with the primary infection had been ill for from two to five days before a report was made to the department of health. During this period there was ample time for exposure of susceptible members of the family to the disease. Only public education on the importance of early diagnosis and rigid isolation and on the contagiousness of scarlet fever can control this situation. The figures also amply show that quarantine in the home as now carried out is inadequate. As for quarantine in the hospital, there is also need for improvement. During the time of the three week quarantine in from 5.4 to 5.9 per cent of all cases of secondary infection the disease developed in the home after the release of the patient with primary infection from a hospital for contagious diseases; during the time of the four week quarantine in 4.6 per cent of the cases of secondary infection the disease was traceable to similar contacts.

In view of these facts, one wonders whether the increase in scarlet fever is not really due to a higher proportion of scarlet fever strains of the hemolytic streptococcus in certain years. Also one must consider whether scarlet fever can be diagnosed when a rash is not present.

In other words, is the same disease or the same strain of infecting organism present in 2 patients with apparently identical infections of the throat, both having cultures positive for hemolytic streptococci, 1 patient having and the other not having a rash? Possibly a strain can change from a rash-producing variety to one that produces no rash, with the result that while the same number of pharyngeal infections are present from year to year, the number of those accompanied with a rash, which are diagnosed as scarlet fever, is variable.

NOTE.—The discussion which followed the presentation of this paper appeared in the report of the transactions of the Chicago Pediatric Society (AM. J. DIS. CHILD. **56:** 224 [July] 1938).

MARBLE BONES

I. CLINICOPATHOLOGIC OBSERVATIONS

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There are over 100 clinical reports of the peculiar condition called marble bones or Albers-Schönberg disease.[1] The original observation of Albers-Schönberg was made on a man 26 years old. Subsequent reports have described patients of all ages, from infancy to adult life. The only feature common to all of the reported cases is the roentgenographic observation of increased density, with loss of detail, of practically all bones of the skeleton. The changes in the blood are at variance; chemical studies made during life are few and incomplete, morphologic observations are rare, and chemical analyses of parts of the skeleton obtained post mortem are lacking. In a case which recently came under our observation circumstances permitted a detailed clinical, pathologic and chemical study. Since these data may contribute to a better understanding of the natural history of this disease, they are presented in some detail.

REPORT OF A CASE

Clinical History.—R. H., a 3½ month old boy, was admitted to the Jewish Hospital on Sept. 5, 1935, with the complaint of insufficient gain in weight and difficulty with feeding since birth. The mother, 32 years old, had had no abortions or miscarriages, and another child, now 6 years old, was living and well; the father was 35 and well. The parents were not related. The mother stated that the infant was born in the Israel-Zion Hospital on May 17, one month prematurely, and weighed 5 pounds and 10 ounces (2,551 Gm.). The head appeared large, but the child otherwise seemed normal. Feeding was always difficult. The baby was never breast fed and had frequent changes of formula. Not more than 2 ounces (59 cc.) of formula was taken at one time. From the age of 2 months, orange juice, viosterol and halibut liver oil were given, but were poorly taken. The baby gained about 3 ounces (85 Gm.) per month. Since July he had had frequent colds in the nose.

On admission to the hospital the patient weighed 9 pounds and 5 ounces (4,224 Gm.); he was poorly developed and poorly nourished, but not cyanotic or dyspneic. The temperature was 98.5 F. and the respiratory rate 54 per minute.

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1. Nussey, A. M.: Osteopetrosis, Arch. Dis. Childhood **13**:161, 1938.

The cervical, axillary, epitrochlear and inguinal lymph nodes were somewhat enlarged. The head was large, with a circumference of 33 cm. The anterior fontanel measured 4 fingerbreadths and bulged slightly. There was some softening about all the sutures, with separation of the coronal and sagittal sutures. The superficial veins of the scalp were markedly dilated. The pupils were equal and regular and did not react to light. The retinas were pale. The bridge of the nose appeared depressed; from the nares a mucoid discharge exuded. The sternum was drawn in; the costochondral junctions were enlarged, and there was a marked Harrison's groove. The lungs were clear, and the cardiac sounds presented nothing unusual. The abdomen was protuberant; the edge of the liver was 2 fingerbreadths below the costal margin; the splenic notch was easily felt, and the edge of the spleen extended to the crest of the ilium. The wrists and ankles appeared somewhat enlarged. Roentgenograms of the skeleton revealed increased density of all the bones, particularly of those of the skull, of the long bones and of the metacarpal and metatarsal bones, some thickening of the periosteum of the long bones and stripping of and deposition of lime salts in the periosteum of the ribs. The metaphysial ends of the long bones appeared frayed and cuffed (fig. 1). Some of the bones showed epiphysial displacement with a metaphysial fracture.

The red blood cell count was 3,270,000 per cubic millimeter and the hemoglobin content 55 per cent; the white cells numbered 13,800, of which 29 per cent were polymorphonuclear leukocytes, 40 per cent lymphocytes, 10 per cent myelocytes and 6 per cent myeloblasts. There were 90,000 blood platelets. The bleeding time was three minutes. The Wassermann and Kahn reactions of the blood were negative, as were those of the father and the mother. The total nitrogen content of the blood was 868 mg. per hundred cubic centimeters, the total protein content 5.2 Gm. and the nonprotein nitrogen content 36 mg. The calcium content of the blood was 8.8 mg. and the phosphorus content 3.1 mg. per hundred cubic centimeters, with a calcium-phosphorus product of 27; the value for phosphatase was 23 units (Bodansky), for cholesterol 153 mg., for sugar 102 mg. and for chlorides 371 mg. per hundred cubic centimeters. The cerebrospinal fluid was clear and contained 67.3 mg. of sugar, 426 mg. of chlorides and 23 mg. of protein per hundred cubic centimeters; the Wassermann reaction was negative. The urine was acid and did not contain albumin or sugar. The Schick, Dick and tuberculin tests gave negative reactions. Wassermann and Kahn reactions were negative on four examinations. A blood count done on September 24, by Dr. Bernard Benjamin, gave the following data: The white blood cells numbered 38,100. A differential count with the supravital technic revealed 22 per cent polymorphonuclear cells, 6 per cent of which were band forms; 1 per cent mature myelocytes; 4 per cent early myelocytes; 1 per cent myeloblasts; 1 per cent basophils; 3 per cent eosinophils; 50 per cent small lymphocytes and 3 per cent large lymphocytes, a total of 53 per cent lymphocytes; 15 per cent monocytes, and 4 per cent monoblasts. The red blood cells revealed moderate anisocytosis and poikilocytosis; the color was approximately normal; the reticulocytes were definitely increased in number.

Treatment.—The child received a mixture of equal parts of evaporated milk and water with dextrimaltose no. 1 in sufficient amount to make 5 per cent of the total volume. In addition, he received a total of 13 ounces (384 cc.) of orange juice, 810 drops of viosterol and exposure to irradiation with the quartz mercury vapor lamp at a distance of about 30 inches (76 cm.) for one hundred and eighty-six minutes. The child vomited one or more feedings daily and probably lost some of the orange juice and viosterol in the vomitus. Ultraviolet irradiation was given to counteract this loss and to insure the availability of the antirachitic factor.

Additional Laboratory Data.—These are given in detail in tables 1 and 2. Chemical studies on the patient's blood serum showed normal nonprotein nitrogen content, a consistently low protein content with a normal albumin-globulin ratio and a rather low normal cholesterol value. The calcium concentration varied from 7.8 to 8.8 mg. in 100 cc. of serum, while the inorganic phosphorus level fluctuated between 2.6 and 3.1 mg., giving a calcium-phosphorus product of 20 to 27, which indicated the presence of active rickets. It is worthy of note that intensive antirachitic therapy which would certainly have favorably affected the

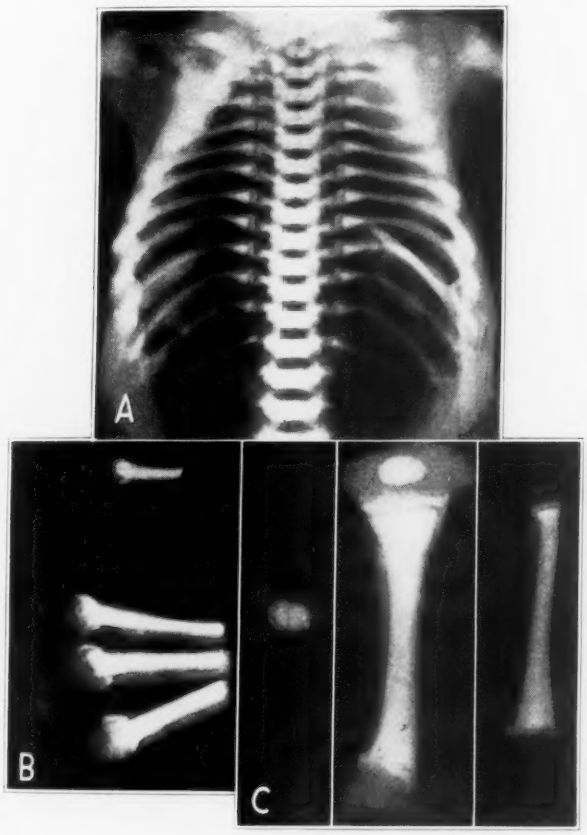

Fig. 1.—Roentgenograms taken post mortem, showing changes in (*A*) the vertebrae and ribs; (*B*) portions of several ribs and (*C*) tarsal bone, tibia and radius.

majority of children with rickets was wholly without effect here, as indicated by the chemical findings in the blood, including the persistence of high phosphatase values, the absence of improvement on roentgen examination and the marked rachitic changes observed post mortem.

Clinical Course.—The child had persistent nasopharyngitis; for two weeks the temperature ranged from 100 to 102 F., but it was normal between September 26 and 30. A few days after admission dulness on percussion and bronchovesicular

TABLE 1.—*Results of Chemical Analyses of the Blood Serum and of the Cerebrospinal Fluid of a Patient with Marble Bones*

Date	9/6	9/30	10/1
Carbon dioxide, volume per cent	.....	52	...
Chlorides, mg. per 100 cc	371	358	...
Nonprotein nitrogen, mg. per 100 cc	36	29	...
Total nitrogen, mg. per 100 cc	868	910	...
Total protein, Gm. per 100 cc	5.20	5.50	...
Albumin, Gm. per 100 cc	....	3.22	...
Globulin, Gm. per 100 cc	....	2.28	...
Albumin-globulin ratio	....	1.41	...
Cholesterol, mg. per 100 cc	153	156	...
Sugar, mg. per 100 cc	102	96	...
Calcium, mg. per 100 cc	8.8	8.2	7.8
Phosphorus, mg. per 100 cc	3.1	3.1	2.6
Calcium-phosphorus product	27	25	20
Potassium, mg. per 100 cc	..	19.5	...
Phosphatase, units	23	28.5	...

Treatment:
Halibut liver oil with viosterol, 30 drops daily, 9/6-9/10, 9/16-10/7
Ultraviolet irradiation, 1½-7 minutes daily, 9/11-10/7

	Cerebrospinal Fluid*	
	9/9	9/16
Sugar	67.3	63
Chlorides	426	430
Protein	23	33

* Values are expressed in milligrams per hundred cubic centimeters.

TABLE 2.—*Results of Hematologic Studies of a Patient with Marble Bones*

Date	9/4	9/5	9/6	9/7	9/11*	9/15	9/27
Hemoglobin, %	60	51	.....	55		80	73
Platelets	.....	.....	80,000	90,000		90,000	40,000
Leukocytes	23,250	26,300	.....	13,840		17,820	26,400
Erythrocytes, millions	3.49	2.46	.....	3.27		4.3	3.66
Color index	.....	.....	.....	0.85			
Bleeding time	.....	.....	5 min.	3 min. 45 sec.			
Clot retraction time	.....	.....	1 hr.				
Coagulation time	.....	.....	3 min.	2 min. (capillary tube) 3 min. (test tube)			
Differential count, %							
Band forms	.....	.....	.....	.....		.....	9
Neutrophils	26	.....	.....	29		32	29
Eosinophils	.....	.....	.....	6		2	
Basophils	.....	.....	.....	.....		2	
Lymphocytes	72	.....	.....	40		30	50
Monocytes	2	.....	.....	2		4	4
"Stab" cells	.....	.....	.....	7			
Myeloblasts	.....	.....	.....	6			
Myelocytes	.....	.....	.....	8		19	3
Metamyelocytes	.....	50	.....	2		11	5
Other data							
Stippling	.....	.....	.....	4 per 100 white cells			
Polychromasia	.....	.....	.....	Very marked			
Megaloblasts	.....	Some	.....	4 per 100 white cells		21	1
Normoblasts	Many	Some	.....	34 per 100 white cells		25	11
Reticulation, %	.....	.....	2.5	2			
Red cell fragility							
Hemolysis began with				0.44% sodium chloride			
Hemolysis was complete with				0.36% sodium chloride			
Control							
Hemolysis began with				0.42% sodium chloride			
Hemolysis was complete with				0.38% sodium chloride			

* Transfusion, 75 cc. of blood.

breathing were noted at the apexes of both lungs posteriorly. These signs later disappeared. The child took his feedings poorly, which necessitated the occasional use of the Levine tube. On October 5 the temperature rose to 103 F. Signs of pneumonia developed, and the infant died on October 8.

Postmortem Roentgenograms.—The ribs showed remarkably uniform symmetric changes. The shaft showed density throughout, with loss of trabecular structure. The metaphysis was separated from the shaft by a zone of rarefaction. Periosteal changes were present on all ribs. The costochondral junctions were club shaped. The humeri showed irregularity of the ends, with displacement of the proximal epiphysis and periosteal changes on both the outer and the inner aspects. The vertebrae showed uniform density (fig. 1 *A*).

Several ribs studied separately showed characteristic density of the shaft, hyperplasia of the periosteum and epiphysial displacement with gross fringing and cupping (fig. 1 *B*).

The radius and tibia showed changes similar to those presented in the other bones, with displacement of the distal epiphysis. The tarsal bones showed a calcified nucleus surrounded by a ring of rarefaction and a somewhat less dense outer zone (fig. 1 *C*).

Necropsy.—The examination was made five hours after death. The body was 53 cm. long and weighed 4.5 Kg. The skin was pale and loose, particularly over the extremities, where it could be lifted into large folds. The head was large and square. The forehead was 5 cm. high; the biparietal diameter was 11 cm., and the occipitofrontal diameter was 15 cm. The scalp was covered with scant, light brown hair. The anterior fontanel was patent and soft, bulged slightly and measured 6.5 by 4.5 cm. The posterior fontanel was closed. The lids of both eyes, especially the left, pitted on pressure. The scleras were clear and the corneas slightly opaque. The pupils were regular, and each measured 0.6 cm. in diameter. The nose was saddle shaped; the septum was straight. There was no discharge from the nose or ears. The lips were pale and slightly crusted. The thyroid gland was not enlarged. The circumference of the chest was 33 cm., the ventrodorsal diameter 9 cm. and the transverse diameter 12 cm. The costochondral junctions were beaded and symmetrically thickened up to a diameter of 1 cm. There was marked flaring of the ribs below the level of the fifth. The abdomen was tense and protuberant and measured 40 cm. in circumference. The testes were in the scrotum. There was no cyanosis and no deformity of the fingers and toes.

The anterior abdominal wall was thin and practically devoid of adipose tissue. The contents of the abdominal cavity bulged into the incision. The peritoneal cavity contained no excess of fluid; its surfaces were smooth and glistening. The two lobes of the liver appeared symmetric, and their anterior surfaces were exposed. The edge of the liver reached 7 cm. below the costal margin in the right midclavicular line and 6.5 cm. below in the left. The diaphragm was at the level of the seventh rib on both sides. The lower pole of the spleen extended 6.5 cm. below the costal margin in the left midclavicular line. The stomach was distended with milky fluid and reached 4 cm. below the edge of the liver in the median line. The layers of the greater omentum were not fused. The mesenteric lymph nodes were conspicuous but not enlarged.

The costal cartilages cut with ease. There were two points of ossification in the sternum: one in the manubrium and one in the body. The thymus covered the space between the anterior margins of the lungs, which were 3 cm. apart. It measured 4 by 2 by 0.5 cm. and weighed 10 Gm. The usual lobulation was noted externally and on the cut surfaces. Both lungs were moderately collapsed.

There was no excess of fluid in either pleural cavity, and the pleural surfaces were smooth and shiny. The pericardial cavity contained no excess of fluid, and the pericardial surfaces were smooth and glistening. The heart measured 5 cm. from base to apex and 5.5 cm. across the base; it weighed 48 Gm. There were no anomalies of the large vessels. The atria, the ventricles, the orifices and their valves presented nothing unusual. Both lungs were air containing throughout; together they weighed 101 Gm.

The spleen kept its shape well; it measured 9 by 5.5 by 4.5 cm. and weighed 88 Gm. Its capsule was smooth, and the cut surfaces were cherry red. The stomach contained about 300 cc. of milky fluid. The mucosa of the stomach and duodenum presented no change. The liver was light brown; it measured 16 by 10 by 6 cm. and together with the stomach, duodenum, gallbladder and pancreas weighed 260 Gm. The lobular markings were distinct on the external surface and, to a lesser degree, on the cut surfaces. The gallbladder was nearly empty; it measured 2.5 by 1 cm., and its fundus failed to reach the inferior margin of the liver by 2 cm. The pancreas measured 7 by 2 by 1.5 cm.; it presented nothing unusual externally or on the cut surfaces. The right adrenal gland measured 3 by 1.7 by 0.5 cm. and the left 3.2 by 2.8 by 0.6 cm.; each weighed 2 Gm. Their external surfaces were light yellow and gyrated; on the cut surfaces the medulla was scant. The right kidney measured 6 by 3 by 2.5 cm. and weighed 31 Gm. The cut surfaces were pale, and the cortical and medullary markings were distinct. The calices, the pelvis and the ureter presented no abnormality. The left kidney resembled the right. The urinary bladder was empty; its mucosa was pale and was thrown into fine rugae. The jejunum was normal. Peyer's patches of the ileum were prominent, as were the lymph follicles of the mucosa of the cecum and of the ascending colon. The rectum presented no change. The tongue, pharynx, esophagus, larynx, trachea and bronchi were not unusual. The inferior and superior tracheobronchial and paratracheal lymph nodes were conspicuous and measured up to 1 cm. in diameter.

The periosteum of the cranium was smooth. Over each frontal prominence was a dark red area, measuring up to 1.5 cm. in diameter. There were several white areas of ossification; those of the frontal prominences measured 3 by 2 cm., and those of the parietal tuberosities, 2 by 2.5 cm. The thickness of the frontal bone was markedly increased, measuring up to 1.2 cm. in the median line and 0.4 cm. on the sides. In the temporal region the thickness of the calvarium was as much as 0.8 cm., and in the occipital region, 0.4 cm. The tabula vitrea and the diploe merged without any distinct line of separation. All the cranial fossae were shallow, especially the anterior fossa. A thick bony plate with a smooth surface, convex toward the cranial cavity, formed the roof of the orbit. The anterior clinoid processes were obliterated. The small wings of the sphenoid bone were thick, and their cranial surfaces were smooth and convex. The sella turcica was shallow, so that the hypophysis was half in the sella and half above it. The dorsum sellae was low and rounded. The posterior clinoid processes were absent. All the foramens for the passage of the cranial nerves and blood vessels were narrowed. Except in the optic foramens, no constriction of the structures passing through the openings was noted. The superior and inferior petrosal, the cavernous, the transverse and the sigmoid sinuses were normal.

The leptomeninx was delicate. The cerebral and cerebellar hemispheres, the cerebral peduncles, the pons and the medulla oblongata were proportionate and symmetric. The convolutions were rounded, delicate and well formed both on the convexity and on the base. The sulci were narrow. Nothing remarkable was

noted about the blood vessels and the cranial nerves. There was no pressure cone of the cerebellum. The cut surfaces of the cerebral peduncles were not unusual. The aqueduct of Sylvius measured 0.3 by 0.2 cm. The cut surfaces of the vermis cerebelli had the usual delicate gyrations. The cavity of the fourth ventricle was not distended, and the pattern of its floor was well preserved. The cut surfaces of the cerebellar hemispheres and frontal sections of the pons and the medulla oblongata disclosed no changes. Frontal sections of the cerebral hemispheres presented the usual pattern of the gray and white matter. The cavities of the lateral ventricles and of the third ventricle were somewhat enlarged,

Fig. 2.—Section of a parathyroid gland. Magnification, × 90.

the former measuring up to 2 cm. in diameter. The pineal body was not conspicuous. No changes were noted in the hypophysis on gross or microscopic examination.

Microscopic preparations through the trachea, esophagus and surrounding structures at the level of the isthmus of the thyroid gland showed variation in the size and shape of the thyroid acini. These were embedded in a scant connective tissue stroma, were lined by cuboid or columnar cells and contained pink-staining colloid. A parathyroid gland which was included was of the usual size (fig. 2). It was surrounded by a delicate connective tissue capsule, with septums subdividing the groups of cell cords and nests. No changes were noted in the trachea and

the esophagus. In preparations from the thymus, well formed lobules were separated by broad bands of loose fibrous connective tissue. The cortical and the medullary portions were distinct. In the latter, Hassall's corpuscles were numerous. In preparations from the liver, spleen, kidneys and lymph nodes, small scattered islands of blood-forming foci were noted; there were no other pertinent changes. No blood-forming islands were identified in preparations from the myocardium, lungs, pancreas, ileum, adrenal glands and the wall of the urinary bladder.

Preparations from the ribs, vertebrae, radius, tibia, calcaneus and calvarium disclosed conspicuous changes. Along the chondro-osseous junction of a rib (fig. 3) the fairly cellular cartilage, with its resting and dividing cells, continued into a zone, about three times the usual thickness, of long and wide columns of foamy

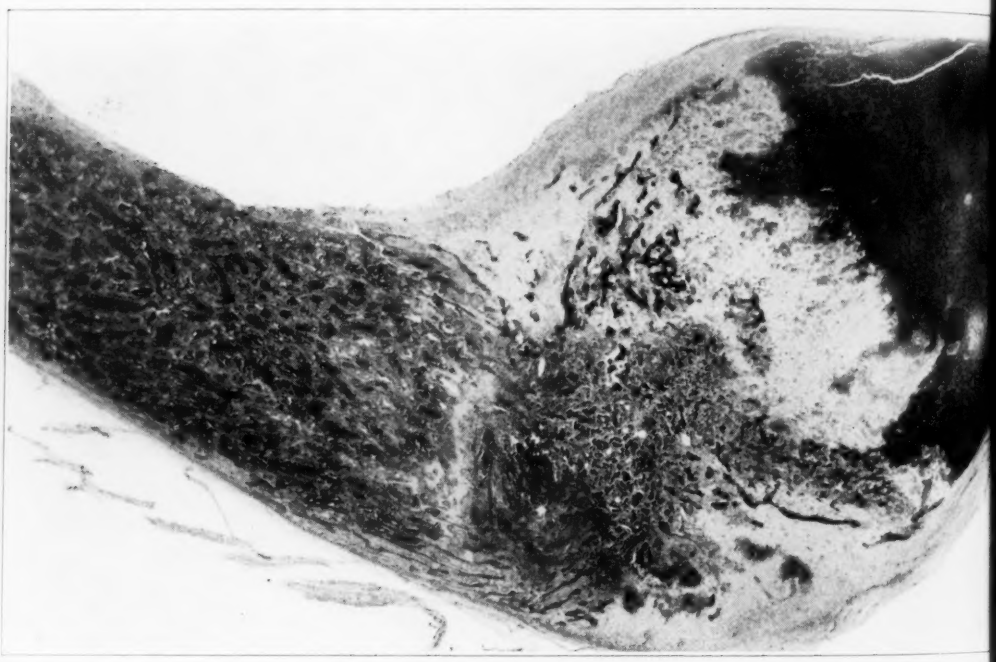

Fig. 3.—Longitudinal section of a rib, showing irregular chondro-osseous junction, wide metaphysis and fracture of the lattice with angulation. Magnification, × 8.5.

cartilage cells separated by a scant, delicate network of the homogeneous ground substance of the cartilage. The latter became coarse and more deeply stained toward the jagged line of contact with the marrow. The marrow formed a band as wide as the zone of the dividing and the foamy cartilage cells. Within this band of marrow tissue were scattered islands of minute bony fragments, bordered by a narrow rim of deeply stained ground substance of the cartilage. In excavations of the latter there were multinucleated giant cells (fig. 4). These chondroclasts were more numerous about the smaller fragments than about the larger. Beyond the band of marrow tissue containing osseous and cartilaginous fragments there were broad bony trabeculae with faintly indicated haversian sys-

tems. The trabeculae were bordered by a thin layer of the ground substance of the cartilage and enclosed rather small marrow spaces. Some of these were filled with loose fibrous connective tissue which contained wide capillaries and others with cellular marrow. In the latter, megakaryocytes, erythroblasts, myeloblasts

Fig. 4.—Section of bone, showing hemorrhage and fragments of calcified material with giant osteoclasts. Magnification, × 250.

and myelocytes were numerous and in good proportion. Beneath the periosteum, on the convex side of the rib, there was an almost continuous thin bony plate. Connected with this and extending almost halfway to the center there was a

network of delicate bony trabeculae with scanty cartilaginous ground substance. Between these trabeculae there were wide communicating marrow spaces, some filled with marrow and others with connective tissue. In occasional areas of the connective tissue there were dense infiltrations of red blood cells. In the remaining half of the osseous tissue the bony trabeculae partly bordered by cartilaginous

Fig. 5.—Chondro-osseous junction of a vertebra. Magnification, × 90.

ground substance formed a broad network with tiny marrow spaces, many of which contained connective tissue rather than marrow. Thus, the concave half of the osseous tissue of the rib had a rather compact structure, whereas the convex half was spongy.

Preparations from frontal sections of the bodies of some of the lumbar vertebrae (figs. 5 and 6) presented a structure similar to that of the concave, compact part of the rib. Broad bony trabeculae partly bordered by a narrow rim of cartilaginous ground substance enclosed many minute and a few large marrow spaces. The larger spaces contained cellular marrow, and the smaller, con-

Fig. 6.—Section of a vertebra, showing network of wide trabeculae with marrow spaces. Magnification, × 110.

nective tissue and occasional cells. The chondro-osseous junction was fairly straight, though in occasional areas the marrow was in direct contact with resting cartilage. The width of the zone of the dividing and the foamy cartilage cells varied, but was at least three times greater than usual.

Preparations from the radius also presented an increase in width of the zone of the dividing and the foamy cartilage cells. The chondro-osseous junction was

irregular. In the zone of ossification the bony lamellae formed a delicate network, enclosing marrow spaces filled with young connective tissue. Multinucleated giant cells about minute osseous fragments were numerous. Under the periosteum, beneath a bony plate, there were large communicating marrow spaces filled with cellular marrow or loose connective tissue, both extensively infiltrated with extravasated blood. Beyond this large, broad, mostly longitudinal bony lamellae bordered marrow spaces filled with cellular marrow. Scattered through the marrow were many megakaryocytes, and toward the periphery of the marrow, rows of multinucleated giant cells.

Preparations from the tibia presented much the same appearance about the chondro-osseous junction as those from the ribs and radius. In the broad zone between the dividing and foamy cartilage cells and the osseous tissue, the marrow was permeated by young connective tissue and infiltrated with red blood cells. Scattered through this marrow were minute cartilaginous and osseous fragments surrounded by multinucleated giant cells. There was no continuous bony layer beneath the periosteum. Beneath this on one side, and extending almost to the center, the bony trabeculae were broad and enclosed few and small marrow spaces. Multinucleated giant cells with three to fifteen nuclei were located in excavations of the bony trabeculae. On the opposite side the bony trabeculae were slender, and the marrow spaces were large. Over extensive areas the marrow was blotted out by extravasated blood in a state of organization.

Preparations from the calcaneus showed the same changes along the chondro-osseous junction as were noted in the ribs, radius and tibia. Large marrow spaces filled with cellular marrow were here more extensive than elsewhere.

Preparations from the calvarium showed broad bony trabeculae, mostly in an arrangement perpendicular to the surface. In the trabeculae were seen wavy blue lines and faint outlines of haversian systems. The surfaces of the trabeculae toward the marrow spaces were ragged, with many osteoclasts in the lacunas. The marrow spaces were fairly large and communicated with one another. They contained loose or dense fibrous connective tissue, with many capillaries and occasional islands of marrow cells. Other spaces were filled with cellular marrow which had the usual variety of cells.

COMMENT

According to Schmidt,[2] it is desirable to separate the cases in which marble bones occur in infancy or in early childhood from those in which the condition appears later in life. He contended that in the adult type of the disease usually the changes in the blood and in the blood-forming organs (osteosclerotic anemia) dominate the picture, while in the childhood type the skeletal changes are paramount. Indeed, in the latter type the changes in the osseous system are so progressive and severe that the afflicted children usually do not survive to reach complete skeletal development.

Our case, as far as can be ascertained, is identical with a considerable number of those reported as to the approximate age of the patient, the roentgenographic appearance of the skeleton and the clinical course of

2. Schmidt, M. B.: Ueber osteosclerotische Anämie und Albers-Schönbergsche Krankheit, Beitr. z. path. Anat. u. z. allg. Path. **77**:158, 1927.

the disease, with blindness and fatal termination.[3] The postmortem observations in our case suggest that the changes in the skeleton about the centers and lines of ossification and the resulting production of a faulty osseous structure were the principal lesions. Whether all the osseous changes were a part of this disease or whether some of the lesions, such as the hemorrhage and the extensive presence of the homogeneous ground substance with lack of calcification, were evidence of superimposed or associated scurvy and rickets cannot be stated with certainty. The changes in the bone marrow were slight and secondary, so that the scattered blood-forming islands in the liver, spleen, kidneys and lymph nodes were perhaps remains from fetal life rather than part of a compensatory mechanism. Of the organs of internal secretion, the thymus, the thyroid, the parathyroid and the adrenal glands presented nothing unusual, nor could any morphologic changes be detected in the hypophysis cerebri.

Many theories have been offered to explain the fundamental nature of this disease. A detailed discussion of these would carry us far beyond the scope of this report. We believe that at this stage of knowledge factual data are more important than theoretic considerations. Consanguinity of the parents, as well as syphilis, was excluded as an etiologic factor in this case. An older child in the family was living and well. The disease was in all probability present at birth, and dietary factors operative during the neonatal period could therefore have played no part in its causation. However, evidences of avitaminosis were present. The child presented a degree of rickets which we had never seen in one of such tender age. Furthermore, the lesion was extremely resistant to therapy. This could not have been due to failure of absorption of the antirachitic factor, since the ultraviolet radiation alone was sufficient to have left its mark on the average child with rickets. This refractory state was relative: We have recently found that huge doses of vitamin D (15,000 U. S. P. XI units) given daily will cure the associated rachitic state in an infant with marble bones. Here, again, the healed lesion roentgenologically resembles that in marble bones rather than normal bone, and the blood calcium-phosphorus product, even after several months of such intense therapy, does not exceed a value of 45 (normal 60). The appearance of the bone suggests a scorbutic lesion, in addition to the lesions of rickets and marble bones, indicating possibly faulty utilization of the antiscorbutic factor. One cannot wholly suppress the thought that the anemia may be due to a similar metabolic defect.

3. McCune, D. T., and Bradley, C.: Osteopetrosis (Marble Bones) in an Infant: Review of the Literature and Report of a Case, Am. J. Dis. Child. **48:** 949 (Nov.) 1934.

It must not be inferred that we consider marble bones itself to be a type of avitaminosis. The metabolic defect, whatever it is, confers on the patient susceptibility to certain avitaminosis, the manifestations of which are modified by the lesion characteristic of marble bones, which not only produces morphologic changes but confers a state of refractoriness to appropriate therapy.

Examination of the various endocrine glands, including the parathyroid, shows no morphologic changes which warrant the assumption of endocrinopathy.

SUMMARY

A case of the typical juvenile form of marble bones (osteosclerosis fragilis generalisata, Laurell and Wallgren; *Marmorknochenkrankheit*, Albers-Schönberg; osteopetrosis, Karshner) has been described with clinical, pathologic, roentgenologic and chemical data.

The significance of these findings has been discussed.

SERUM CALCIUM IN THE NEWBORN

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In a preliminary communication [1] we outlined our objective in studying the serum calcium in the neonatal period. If there were a constant relation between the serum calcium of the cord blood and the serum calcium of the peripheral blood of infants in the first few weeks of life one might predict and prevent tetany of the newborn. If a low value for the serum calcium of the cord blood were associated regularly with a low value for the calcium in the blood of infants under 2 weeks of age, the occurrence of tetany might be anticipated. Examination of the cord blood and the peripheral blood of normal infants revealed a very different relationship and led us to inquire into the factors which govern the calcium level in neonatal life.

That the cord blood has a higher level of calcium than the maternal blood is known. Numerous authors have recorded values from 1 to 3 mg. per hundred cubic centimeters higher on the fetal than on the maternal side of the placenta. Needham tabulated their results.[2] Diffusion cannot account for this difference in level. Bokelmann and Bock [3] stated the belief that the placenta acts as a storehouse for calcium from which the fetus withdraws increasing amounts, particularly during the last three months of gestation. The data they presented are suggestive, but complete proof of their contention is still lacking. Schick [4] pointed out that the fetal circulation is a closed circuit. The fetus excretes calcium, in extremely small amounts, only

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1. Denzer, B.; Reiner, M., and Vogel, P.: Calcium Studies in the Newborn, Proc. Soc. Exper. Biol. & Med. **38**:492 (May) 1938.

2. Needham, J.: Chemical Embryology, New York, The Macmillan Company, 1931, p. 1527.

3. Bokelmann, O., and Bock, A.: Ueber die Zustandsform des Calciums im Serum während die Gestationszeit: Die Beziehungen zwischen Mutter und Fetus, Arch. f. Gynäk. **133**:739, 1928.

4. Schick: Personal communication to the authors.

in the meconium [5] and deposits calcium in the bones. Some part of the calcium may return through the placenta to the mother, A larger part circulates in the closed circuit of the fetal circulation. By such a mechanism the high level of calcium might be explained. It would be interesting to determine whether the low calcium content in the meconium changes gradually to a higher level in the feces after interruption of the previously existing outlet through the placenta.

The calcium level of the maternal blood still has a certain influence on that of the cord blood. Mull [6] has shown that, on the whole, the height of the calcium level of the fetal blood depends on the concentration of calcium in the maternal blood (table 1). It should be emphasized that even relatively low figures for maternal calcium are still associated with levels in the cord blood above the amount accepted as normal for later infancy, 10 mg. per hundred cubic centimeters.

Our work traced the course of the variations in calcium content from birth to the tenth day of life.[7] To determine whether the

TABLE 1.—*Summary of Calcium Levels in Maternal and in Cord Blood* *

Maternal Blood Calcium		Cord Blood Calcium	
Number of Cases	Range, Mg. per 100 Cc.	Average, Mg. per 100 Cc.	Range, Mg. per 100 Cc.
1	8.0-8.49	10.53	
14	8.5-8.99	10.32	9.00-11.00
25	9.0-9.49	10.83	9.96-11.93
16	9.5-9.99	11.58	10.54-13.10
8	10.0-10.49	11.86	10.90-12.50

* Condensed from Mull.[6]

calcium content of the cord blood represents that of the blood of the newborn infant, estimations were made immediately after birth in 6 cases. Table 2 shows the calcium content of cord blood and of blood taken from infants within five hours after birth. The differences are slight, which permits the assumption that serum calcium values of the cord blood represent the calcium content of the blood serum of the newborn infant.

The striking feature of the calcium level during the first ten days of life is the deep depression that takes place during the first four days (table 3).

5. Brock, J.: Biologische Daten für den Kinderarzt: Grundzüge einer Biologie des Kindesalters, Berlin, Julius Springer, 1932, pp. 212-213.

6. Mull, J. W.: Variations in Serum Calcium and Phosphorus During Pregnancy: Effect on Fetal Circulation, J. Clin. Investigation **15**:513 (Sept.) 1936.

7. The Clark-Collip modification of the Kramer-Tisdall method was used to determine the serum calcium, and the Kuttner-Lichtenstein method was employed for the determinations of phosphorus. (Clark, E. P., and Collip, J. B.: A Study of the Tisdall Method for the Determination of Blood Serum Calcium, J. Biol. Chem. **68**:461, 1925. Kuttner, I., and Lichtenstein, L. J.: Micro-Colorimetric Studies: II. Estimation of Phosphorus, ibid. **86**:671, 1930).

Thereafter the curve gradually rises; it does not reach the level of the calcium content of the cord blood, but by the seventh day it attains a point a little higher than the average level of later infancy. The two series of cases studied by us are almost identical as far as the initial postnatal drop is concerned. Thus, in the first series [1] the calcium level at the third and fourth day of life was 1.21 mg. lower than the level of the cord blood of the same infants. In the two series there was the same upward trend toward the tenth day of life, but in the first series the calcium level reached a higher point, 11.5 mg., than in the cases presented here, in which the value rose to 11.37 mg. There

TABLE 2.—*Determinations of Calcium in Cord Blood and in Blood Taken Within Five Hours of Birth*

Case No.	Time, Hours	Cord Blood Calcium	Baby's Blood Calcium
79	5	11.58	11.58
88	1	11.06	10.87
87	4	10.95	10.68
89	2	10.78	10.48
90	2	12.05	11.27
91	1	11.18	11.08

* Values are expressed in milligrams per hundred cubic centimeters.

TABLE 3.—*Determinations of Calcium in Cord Blood and in Blood Taken During the First Ten Days of Life* *

Days	Number of Cases	Cord Blood Calcium		Peripheral Blood Calcium		Mean Difference (Peripheral — Cord Blood)
		Mean	Range	Mean	Range	
1 and 2	21	11.61	9.50-13.20	10.48	8.75-11.88	—1.13
3 and 4	19	11.82	10.80-14.20	10.75	8.60-12.80	—1.06
5 and 6	23	11.52	9.50-13.50	10.72	8.96-13.20	—0.80
7 and 8	19	11.13	9.00-13.59	11.04	9.20-14.02	—0.09
9 and 10	9	11.57	10.60-12.95	11.37	10.00-14.50	—0.20
Total	91	11.53	9.00-13.12			

* Values are expressed in milligrams per hundred cubic centimeters.

were 47 cases in the first series, and the infants were predominantly white; in the present series the infants were predominantly Negro, and 91 cases were studied. The differences were in degree only; the values showed the same downward trend in the first four days of life and the subsequent rise (table 4).

An explanation was sought for this fall in the calcium content. The weight at birth was not a factor. Infants weighing 5 or 6 pounds (2,267 or 2,721 Gm.) showed the same drop in the calcium level as those weighing from 7 to 9 pounds (3,175 to 4,082 Gm.). The type of feeding was not a factor. Only 1 baby was fed completely by bottle. The rest received a bottle only at 2 a. m.; otherwise all the infants were breast fed. The feeding routine consisted of twelve hours of starvation, twelve hours of feeding a 5 per cent solution of dextrose in water and thereafter breast feeding every four hours. The degree of loss

in weight cannot be correlated with the extent of the drop in the calcium content; thus, the babies that lost only 4 ounces (113 Gm.) in weight suffered the same degree of decrease in the calcium content as those that lost 8 ounces (227 Gm.) or more. An attempt was made to relate the percentage of loss in weight to the percentage of drop in the calcium level, but no relationship existed. Race was not a factor. Thus, weight at birth, loss of weight, feeding and race afforded no explanation for the drop in calcium values.

Of course, there was a relation between the height of the calcium level in the cord blood and the subsequent fall. Thus, a low level of calcium in the cord blood was followed by only a slight drop during the first few days of life. Had the extreme degree of depression in calcium taken place in the cases in which the calcium content of the cord blood was low, the tetanic level for calcium would have been reached. There were 3 cases in which the level in the cord blood was

TABLE 4.—*Summary of Calcium Values for Infants Included in the Present and in the Preliminary Report* *

Days	Total Number of Cases	Cord Blood Calcium Mean	Peripheral Blood Calcium Mean	Mean Difference (Peripheral — Cord Blood)
1 and 2	32	11.66	10.56	—1.10
3 and 4	35	11.91	10.77	—1.14
5 and 6	31	11.61	10.93	—0.69
7, 8, 9 and 10	40	11.18	11.25	+0.07
	138	11.57		

* Values are expressed in milligrams per hundred cubic centimeters.

between 9 and 9.75 mg. per hundred cubic centimeters. In 1 of these the value fell to 8.75 mg. on the first day of life, but rose to 9.02 mg. on the sixth day. In the second case the value was the same on the sixth day as it was at birth. In the third case the value rose 0.7 mg. per hundred cubic centimeters between birth and the eighth day of life. The factors which prevent the calcium content from falling to the tetanic level are as yet unknown.

Because of the relation between serum protein and serum calcium, studies on serum protein were made. The refractometric method (Neuhausen formula) was used in order to avoid the withdrawal of large quantities of blood.[8] The results were remarkably constant. No

8. The relation between protein and calcium and the degree of ionization of the calcium as calculated by the method of McClean and Hastings apparently do not hold for cord blood and for infants' blood. This has been observed by Andersch and Oberst for a series of 25 newborn infants (McClean, F. C., and Hastings, A. B.: The State of Calcium in the Fluids of the Body, J. Biol. Chem. **108**:285, 1935. Andersch, M., and Oberst, F. W.: Filterable Serum Calcium in Late Pregnant and Parturient Women and in Newborn, J. Clin. Investigation **15**: 131, 1936).

correlation can be found between the steady level of protein and the fluctuations in the calcium level (table 5).

The inorganic phosphorus content of maternal as compared with that of fetal blood has been studied. The results of all authors have shown higher phosphorus values in the fetal blood. Needham tabulated the data.[9] It is interesting that so many of the investigators studied whole blood rather than plasma. No doubt this preference rests on technical considerations. Hemolysis and standing tend to cause higher figures for serum phosphorus. In the newborn the effect of hemolysis on determinations of phosphorus is particularly important: Hemolysis occurs normally in the newborn (icterus neonatorum),[10] and the red cells are particularly fragile.[10] Thus several circumstances favor hemolysis and render determinations of phosphorus relatively inaccurate.

In our work, when insufficient blood was obtained from an infant, the calcium content was determined in preference to the phosphorus

TABLE 5.—*Determinations of Protein in Cord Blood and in Peripheral Blood* *

Days	Number of Cases	Cord Blood Protein		Peripheral Blood Protein		Mean Difference (Peripheral—Cord Blood)
		Mean	Range	Mean	Range	
1 and 2	17	6.06	5.15-7.43	6.03	5.10-7.02	—0.03
3 and 4	20	6.15	5.26-7.32	5.89	5.15-6.67	—0.26
5 and 6	21	6.02	5.31-6.65	6.02	5.10-7.01	0.00
7 and 8	15	5.96	5.31-6.70	5.93	5.10-6.60	—0.03
9 and 10	6	5.88	5.52-6.75	5.96	5.37-7.53	+0.08
	79	6.04	5.15-7.43			

* Values are expressed in grams per hundred cubic centimeters.

content. Blood that showed any signs of hemolysis was discarded. The blood of an infant was drawn from the internal jugular vein and was examined within two hours. Specimens of cord blood which could not be examined within eight hours of birth were discarded, even though no evidence of hemolysis was present.

In general the phosphorus values are higher in the blood of newborn infants than in cord blood or in the blood of older infants. The average value for cord blood in 41 cases was 6.06 mg., and for blood taken postnatally in the same cases, 7.11 mg., a difference of 1.05 mg. per hundred cubic centimeters. An attempt to analyze these figures further failed to show any significant trend (table 6).

Thus, the average of estimations made in 9 cases on the first day of life was 6.95 mg., a rise of 1.52 mg. per hundred cubic centimeters

9. Needham,[2] p. 1521.

10. Goldbloom, A., and Gottlieb, R.: Icterus Neonatorum, Am. J. Dis. Child. **38**:57 (July) 1929.

above the level in cord blood; the average in 11 cases on the seventh and eighth days was 6.88 mg., a rise of 0.65 mg. above the level in cord blood. Similar results are noted if one compares the average of the first four days with the average of the fifth to the ninth day; the average for the first four days was 6.66 mg., and that for the succeeding four days, 7.11 mg.

The comparison of the phosphorus with the calcium values is of particular interest. In 13 cases in which the calcium content of the infant's blood was under 10 mg. per hundred cubic centimeters the

TABLE 6.—*Determinations of Phosphorus in Cord Blood and in Peripheral Blood**

Days	Number of Cases	Cord Blood Phosphorus		Peripheral Blood Phosphorus		Mean Difference (Peripheral – Cord Blood)
		Mean	Range	Mean	Range	
1 and 2	14	5.71	4.4-7.1	7.22	6.0-8.4	+1.51
3 and 4	8	6.15	4.9-7.3	6.94	6.1-8.0	+0.79
5 and 6	8	6.34	4.8-7.4	7.42	5.7-8.9	+1.08
7 and 8	11	6.23	4.0-8.6	6.88	6.0-8.0	+0.65
	41	6.06	4.0-8.6	7.11	5.7-8.9	

* Values are expressed in milligrams per hundred cubic centimeters.

TABLE 7.—*Determinations of Phosphorus in Cases in Which the Calcium Level Was Under 10 Mg. per Hundred Cubic Centimeters**

Case No.	Calcium	Phosphorus
65	8.67	6.00
2	8.75	6.40
63	8.96	8.70
3	9.02	6.50
49	9.20	6.00
28	9.60	7.70
92	9.60	8.00
80	9.64	7.69
20	9.70	8.00
12	9.70	6.00
76	9.78	9.37
44	9.78	6.00
64	9.95	6.06
Mean	9.41	7.11
Median	9.31	7.69

* Values are expressed in milligrams per hundred cubic centimeters.

phosphorus values were not high; indeed, they averaged only 7.11 mg., the average phosphorus value for the entire group (table 7).

These data are emphasized because of the significance placed on relative calcium and phosphorus values. It is generally accepted that hypoparathyroidism manifests itself by the inadequate excretion of phosphorus through the kidneys, by a resultant absolute or relative excess of phosphorus in the blood and secondarily by a fall in the calcium content. If the postnatal fall in the calcium level which we have demonstrated were associated regularly with an appreciable elevation in the phosphorus level, the assumption of hypoparathyroidism might be justi-

fied. We do not deny the possibility that a temporary depression in parathyroid function may exist during the early neonatal period, but we do not believe the available data to be definite proof thereof.

Bakwin, studying the same subject, came to different conclusions. It seems advisable to explore the possible reasons for these differences. Bakwin wrote:[11]

> Coincident with the variations in the serum calcium content there is a steady rise in the serum phosphorus content from a mean value of 5.98 mg. per hundred cubic centimeters for placental serum to 6.14 mg. from the third to the fifth day and 6.84 mg. from the sixth to the tenth day.

The increase in the phosphorus content of the blood of the infants from 3 to 5 days of age over that of the cord blood was only 0.16 mg. per hundred cubic centimeters, a truly insignificant amount, and the values for the next five days were only 0.7 mg. higher. This slight variation seems to have still less validity when one traces the origin of the data used for comparison. The figures for cord blood phosphorus were taken from the paper by Mull,[6] based on 60 determinations made in a clinic in Cleveland. These were compared with 54 estimations made on other infants; in other words, the phosphorus values for cord and for postnatal blood were those for different groups examined by different workers and not necessarily by the same method. The variations in the phosphorus values obtained by different authors and the natural hazards involved in the tests for phosphorus in the blood of newborn infants render such a comparison of little value. Thus, had Bakwin chosen the figures for fetal phosphorus which were compiled by other authors for comparison with his own results for postnatal blood, the conclusions might have been different.

There must be some mechanism which prevents the initial drop in the calcium content from reaching tetanic levels. The high calcium level at birth in itself supplies a margin of safety. Even a fall of 1.5 to 2 mg. is not sufficient to depress the calcium level much below 10 mg. per hundred cubic centimeters, the estimated normal value for later infancy. When the calcium level of cord blood is below 10 mg. per hundred cubic centimeters, failure of the calcium content of peripheral blood to reach the tetanic level postnatally must be due either to absence of the initial depression of the calcium level or to some other compensating mechanism. Possibly the tendency to acidosis characteristic of the newborn may raise the antitetanic capacity of calcium.[12] Breast

11. Bakwin, H.: Pathogenesis of Tetany of the New-Born, Am. J. Dis. Child. **54**:1211 (Dec.) 1937.

12. Marples, E., and Lippard, V. W.: Acid-Base Balance of New-Born Infants: A Consideration of the Low Alkaline Reserve of Normal New-Born Infants, Am. J. Dis. Child. **44**:31 (July) 1932.

feeding also combats tetany. It is interesting in this connection that no cases of tetany in Negro infants have been reported and that Negro babies comprised 90 per cent of our present series; practically all of them were almost completely breast fed, and no case of tetany was observed among them.[13] On the other hand, cow's milk is tetanogenic and tetany of the newborn is a disease of private practice, in which it is noted that many or most babies are fed artificially, as Bakwin has pointed out. The parathyroids may be a contributory factor in one of two ways: Either they do not function at all in intrauterine life and begin to be active only toward the second week of postnatal life, or their function is temporarily depressed after birth. There still may be some relation between the calcium levels of maternal, cord and postnatal blood. The routine determination of the calcium contents of maternal and of cord blood and subsequent postnatal studies of the blood calcium of those infants whose cord blood was extremely low in calcium might throw light on the pathogenesis of tetany.

SUMMARY

1. A study of the calcium level in the cord blood and of the blood calcium curve of the neonatal period has been made.

2. There is a distinct drop in the calcium level of the blood during the first four days of life, with a subsequent slow rise to a point slightly above the average level of later infancy. This depression of the calcium content is not related to race, weight at birth or neonatal loss of weight.

3. The inorganic phosphorus content of the blood during the neonatal period is higher than the phosphorus content of the cord blood but shows no definite constant curve.

4. The protein level of the blood remains constant during the neonatal period and therefore cannot affect the level of the available ionizable calcium.

5. The data derived from a comparison of calcium and phosphorus curves in the neonatal period do not supply an adequate explanation of tetany neonatorum.

Dr. Morris Gleich, director of the pediatric service of the Harlem Hospital, allowed us to obtain the blood used for this study.

2 West Eighty-Ninth Street.

1 East One-Hundredth Street.

73 East Ninetieth Street.

13. During the period of study there were no convulsions of any kind in the nursery.

FACTORS INFLUENCING APPEARANCE OF CENTERS OF OSSIFICATION DURING EARLY CHILDHOOD

CARL C. FRANCIS, M.D.
CLEVELAND

In a previous paper Werle and I [1] presented a schedule for date and sequence of appearance of centers of ossification in young children. It is the purpose of this report to show how the epiphysial rating may be used as a measure of constitutional health and how specific disturbances affect the schedule.

The centers at the wrist are particularly sensitive to disturbance and by their several stages of progress betray a previous disturbance in health. Roentgenograms of the left hand and wrist of each of several 5 year old boys, together with a brief health report on each, illustrate how the carpal area records fluctuations in health.

The left hand of the first of these boys at the age of 5 years is shown in figure 2. The boy was weaned at 6 weeks, and there was considerable difficulty in finding a suitable substitute formula. During most of his first year he suffered from slight malnutrition. At 4 months he had a severe cold with otitis media; at 6 months he had persistent diarrhea which recurred from 11 to 13 months. He improved during his second year but at 21 months had intestinal influenza, followed by otitis media at 28 months. During his fourth year he had no illnesses. At 4 years and 2 months he had a cold, and at 4 years and 4 months, just after another and more severe cold, the tonsils and adenoids were removed.

This entire health record can be interpreted by a careful examination of the roentgenogram (fig. 2), which shows all hand and wrist centers which should begin to ossify by the age of 1 year (fig. 1) to be present, well mineralized and of appropriate size and contour. Earlier roentgenographic records of this child showed that even these centers were at first retarded in ossification, but by the age of 5 years they had attained the appropriate developmental stage. Centers for the heads of the fourth and the fifth metacarpal bone had obviously been interrupted in their growth. Centers for the epiphyses of the first phalanx of the thumb, the base of the first metacarpal bone, the second phalanx of the

From the Laboratory of Anatomy and Associated Foundations, the Western Reserve University School of Medicine.

1. Francis, C. C., and Werle, P. P.: The Appearance of Centers of Ossification from Birth to Five Years, Am. J. Phys. Anthropol. **24**:273-301, 1939.

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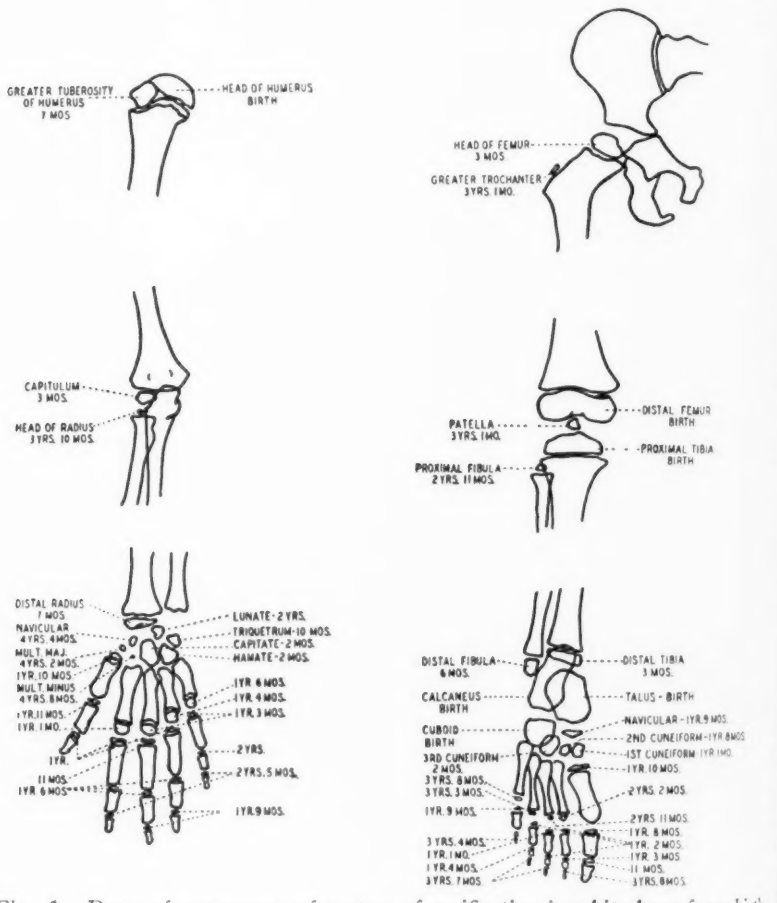
second finger and the lunate bone were likewise poorly formed. All these evidences of disturbance betray the physical debility following the intestinal influenza at 21 months. At the time the roentgenogram was taken the epiphysial center for the distal phalanx of the fifth finger had not yet appeared, although its companion, that for the distal phalanx of the index finger, had begun to ossify. The missing center records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HEAD OF RADIUS 3 YRS. 10 MOS.
PATELLA 3 YRS. 1 MO.
DISTAL FEMUR BIRTH
PROXIMAL TIBIA BIRTH
PROXIMAL FIBULA 2 YRS. 11 MOS.
DISTAL RADIUS 7 MOS.
NAVICULAR 4 YRS. 4 MOS.
MULT. MAJ. 4 YRS. 2 MOS.
1 YR. 10 MOS.
MULT. MINUS 4 YRS. 8 MOS.
1 YR. 11 MOS.
1 YR. 1 MO.
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LUNATE - 2 YRS.
TRIQUETRUM - 10 MOS.
CAPITATE - 2 MOS.
HAMATE - 2 MOS.
1 YR. 6 MOS.
1 YR. 4 MOS.
1 YR. 3 MOS.
2 YRS.
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1 YR. 9 MOS.
DISTAL FIBULA 6 MOS.
DISTAL TIBIA 3 MOS.
CALCANEUS BIRTH
TALUS - BIRTH
CUBOID BIRTH
NAVICULAR - 1 YR. 9 MOS.
3RD CUNEIFORM 2 MOS.
2ND CUNEIFORM - 1 YR. 8 MOS.
1ST CUNEIFORM - 1 YR. 1 MO.
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1 YR. 1 MO.
1 YR. 3 MOS.
1 YR. 4 MOS.
11 MOS.
3 YRS. 7 MOS.
3 YRS. 8 MOS.

Fig. 1.—Dates of appearance of centers of ossification in white boys from birth to 5 years of age.

the disturbance occasioned by otitis media at the age of 2 years and 4 months. The three carpal bones which begin to ossify in the fifth year, the multangulum majus, the multangulum minus and the navicular, were missing as a result of the health disturbance of the early months of that year.

By the time he had reached 5 years of age this boy was not a physically retarded child. When his roentgenograms are compared with

those of Todd's "Atlas of Skeletal Maturation"[2] the metaphyses are quite up to the standard. The same is true of those carpal centers and epiphyses which should ossify before the age of 1 year, that is, those which had had sufficient time to recover from the earlier delay.

Figure 3 is the roentgenogram of the left hand of another boy aged 5 years. This roentgenogram shows that all centers are well ossified except those for the multangulum majus, the navicular and the multangulum minus bone, centers which should begin to ossify at 4 years

Fig. 2.—Roentgenogram of the left hand of a boy aged 5 years. Note the evidences of retarded ossification due to disturbances in health.

2 months, 4 years 4 months and 4 years 8 months respectively. The health record of this boy shows that he had no serious illnesses until the age of 3 years and 5 months, when he suffered a severe streptococcic infection; this was followed four months later by measles and mumps and in another four months (at the age of 4 years and 1 month) by tonsillectomy and adenoidectomy. When the boy reached his fifth

2. Todd, T. W.: Atlas of Skeletal Maturation: I. The Hand, St. Louis, C. V. Mosby Company, 1938.

birthday he was fully restored to good health, but the roentgenograms show that the ossific centers which should have appeared during the fifth year were delayed, while centers which were not retarded in their date of appearance continued to grow without visible interruption. On the original roentgenogram can be seen three transverse lines on the lower part of the radius: the one farthest from the metaphysis was due to the sore throat; the middle one was due to measles and mumps, and the most distal one, caused by the operation, was very faint, indicating that this interruption was less severe than the interruptions due to the preceding illnesses.

Fig. 3.—Roentgenogram of the left hand of another boy aged 5 years.

Figure 4 is a roentgenogram of the left hand of a boy who, though free from any serious infection, had slight signs of respiratory allergy at 2 years, mild hay fever at 3 years, and, in the summer of his fifth year, marked hay fever. He had slight eczema every winter, which became more marked the winter before his fifth birthday. The allergy, increasing steadily in severity up to the fifth birthday, actually interfered with skeletal development, so that outlines of ossification which should

have appeared after the fourth birthday are absent in the roentgenogram. Note also that the center for the lunate bone is missing, though the other 2 year center, that for the epiphysis of the second phalanx of the fifth finger, is distinctly ossified. This illustrates clearly the greater influence on the primary centers of fluctuations in health. The mild allergic reactions in the summer of his second birthday held back the development of the lunate bone but not that of the epiphysis of the second phalanx of the fifth finger.

Fig. 4.—Roentgenogram of the left hand of a third boy aged 5 years. This child suffered from allergy which interfered with skeletal development.

Figure 5 is a roentgenogram of the left hand of another boy aged 5 years. This boy had no illnesses except mild coryza at 4 years and 2 months and again at 4 years and 4 months. The roentgenogram shows every center ossified which should be ossified at 5 years, but the centers for the multangulum minus and the navicular bone are small. After the infections of the respiratory tract there was a slight delay in ossification, but by the fifth birthday the centers had appeared. Thus quickly

in constitutionally robust children the record of mild misadventure is obliterated. It is only in the physically debilitated that the record may still be read after many months.

We have found in our developmental study that children differ widely in their ability to adjust to diet. The skeleton is a sensitive register of progress in this adjustment. The epiphysial rating is a particularly valuable indicator of the building up and maintenance of constitutional health.

Fig. 5.—Roentgenogram of the left hand of a fourth boy aged 5 years. Every center is ossified which should be ossified at that age, but the centers for the multangulum minus and the navicular bone are small.

Epiphysial ossification is retarded by any disturbance of metabolic balance. In infants the difficulty of gastrointestinal adjustment to food is the most frequent cause of disturbed metabolism. Difficulties of gastrointestinal adjustment may be expressed in many ways: in failure to gain steadily in height and weight; in poor mineralization of bone and light muscular shadows on roentgenograms; in slow and erratic epiphysial ossification; in constipation or diarrhea; in colic, gas and

vomiting, and in cutaneous manifestations, such as cradle cap, rashes or eruptions on the face and body.

We have prepared charts of developmental growth of several children to show the relation between epiphysial rating and other measures of developmental growth. The chart for each child shows the status of growth at examinations made at 3, 6, 9, 12 and 18 months of age. Pertinent data concerning feeding and illnesses are recorded on the charts.

The first column in each chart represents the child's chronologic age in months; the second and third columns represent his height age and weight age in months, and the fourth column represents his

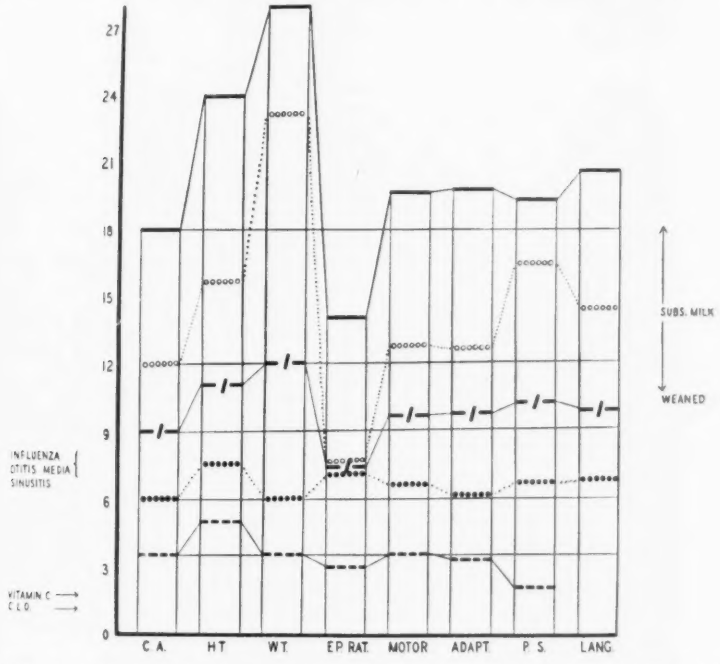

Fig. 6.—Chart of developmental progress of a white boy born May 24, 1932. The initial letters used as abbreviations in the chart are to be interpreted as follows: C.L.O., cod liver oil; C.A., chronologic age; P.S., personal-social rating determined by the Gesell psychologic test as modified by Anderson.

epiphysial rating assessed on our standards. The last four columns record the child's rating on the four parts of our routine psychologic examination, which consists of tests of various phases of psychomotor development. These are modifications by Dr. L. Dewey Anderson of Gesell's tests for the infancy period.

In estimating the age equivalent of each aspect of development we have used standards calculated from the children enrolled in our own series; therefore, each child is compared with other Cleveland children of superior physical and economic status.

The child whose record appears in figure 6 at 3 months showed the satisfactory development of a well child born at full term of healthy parents. The gastrointestinal tract had adjusted itself without difficulty, and there was ample breast milk. Orange juice and cod liver oil were given early and were well tolerated. On examination at the age of 6 months there were well balanced gains. This child, with a good start in life, had the misfortune to contract a disease of severe constitutional effect between the second and third examinations, namely, severe influenza at 7 months. The examination at 9 months showed no disturbance of weight and little retardation in stature but did show marked

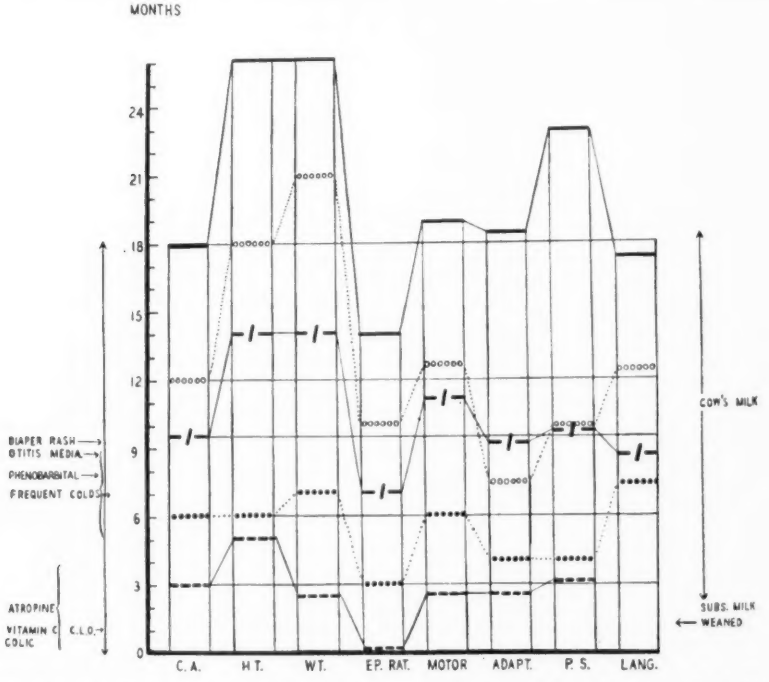

Fig. 7.—Chart of developmental progress of a white girl born Feb. 19, 1933. The initial letters used as abbreviations in the chart are to be interpreted as follows: C.L.O., cod liver oil; C.A., chronologic age; P.S., personal-social rating determined by the Gesell psychologic test as modified by Anderson.

interruption in epiphysial rating, which had not increased since the preceding examination. During a convalescent period, as shown by examination at 12 months, weight and height made excellent gains. All retained mineral had been required for already ossified areas and growing shafts, and epiphysial rating was therefore still retarded. By 18 months mineral could be released for the new centers, and the epiphysial rating therefore rose. The child might now be certified as in good constitutional health in the terms of this standard appraisal.

In such an infant, who has made a satisfactory gastrointestinal adjustment, illness is followed by a definite schedule of convalescence. Weight recovers first, then stature and last of all the mineral metabolism as indicated by epiphysial rating. There need be no obvious disturbance of psychomotor progress.

The girl whose record is given in figure 7 was a child born at full term with a gastrointestinal maladjustment betrayed by pylorospasm resulting in projectile vomiting. There was considerable difficulty in finding a satisfactory substitute for breast milk. Small doses of atropine sulfate were necessary to relieve the spasm and make it possible for the baby to retain its food. Once the adjustment was attained, nutritional and developmental progress continued without interruption. Other evidence of inadequate adjustment was expressed in the skin as cradle cap and diaper rash and in susceptibility to disturbance (particularly of the respiratory tract), such as frequent colds and disease of the middle ear. Children of this type are usually not retarded in stature progress, though weight may fail to show adequate increase and skeletal mineral is always poor. Psychomotor progress is erratic and may be less satisfactory at 18 months than in this child, in whom it was fortunately maintained.

Not every child gains so rapidly in height and weight. One must remember the influence of heredity in producing a child small at birth whose gains in stature, though satisfactory, still leave the height less than standard for the age (fig. 8). If the diet is adequately supplemented by minerals and vitamins, as in the case of the child whose record is shown in figure 8, progress is often maintained despite an original gastrointestinal maladjustment which shows itself merely as slight or transient eczema; hence the tremendous gain in epiphysial rating between the second and the third examination. The diet, rich in mineral, had been supplemented with daily doses of dicalcium phosphate ($Ca\ HPO_4$). The demands of growth being relatively small, there was an abundance of available mineral for utilization in ossification of epiphysial cartilages.

Figure 9 shows the developmental history of a girl who made only moderate gains in stature but whose diet was exceptionally well supplied with vitamins and minerals. In this case there was an early and rapid advance in epiphysial rating. A small amount of vitamin will protect a child from disease due to vitamin deficiency, but, as Sherman [3] has insisted, this is not enough for the American child, who is not merely to be protected from gross disease but to be endowed with optimal health.

3. Sherman, H. C.: Chemistry of Food and Nutrition, ed. 5, New York, The Macmillan Company, 1937.

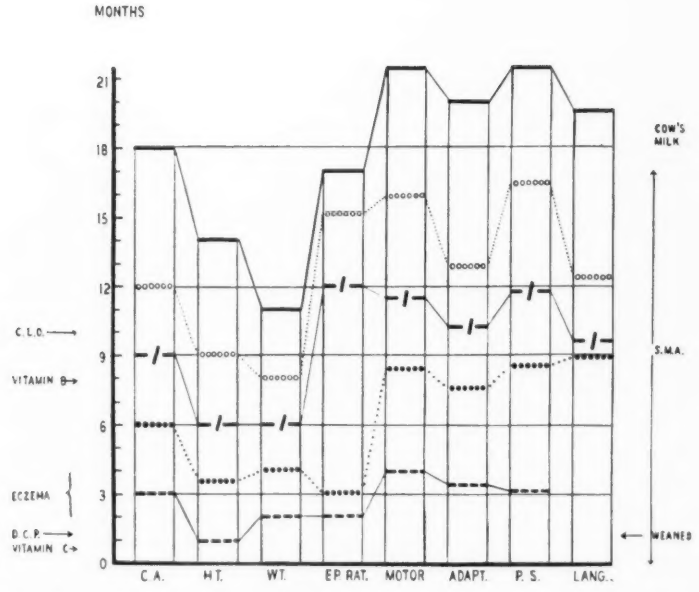

Fig. 8.—Chart of developmental progress of a white girl born Feb. 21, 1933. The initial letters used as abbreviations in the chart are to be interpreted as follows: C.L.O., cod liver oil; D.C.P., dicalcium phosphate; C.A., chronologic age; P.S., personal-social rating determined by the Gesell psychologic test as modified by Anderson; S.M.A., synthetic milk adapted.

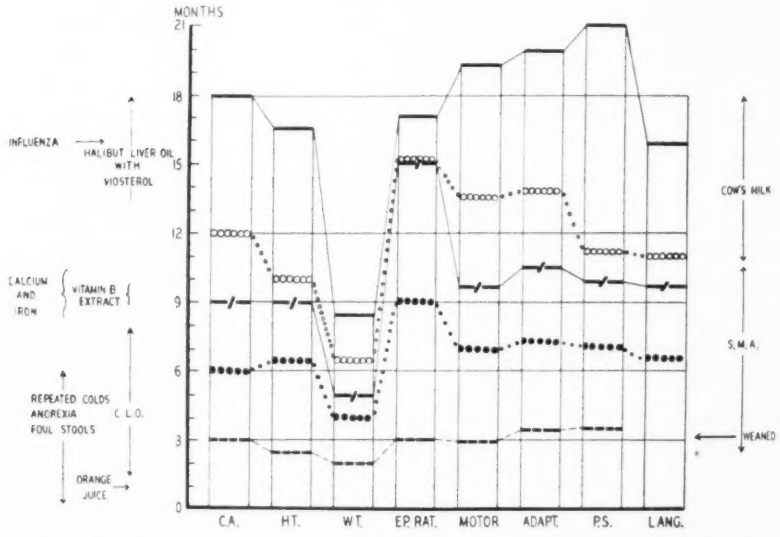

Fig. 9.—Chart of developmental progress of a white girl born Aug. 22, 1931. The initial letters used as abbreviations in the chart are to be interpreted as follows: C.L.O., cod liver oil; C.A., chronologic age; P.S., personal-social rating determined by the Gesell psychologic test as modified by Anderson: S.M.A., synthetic milk adapted.

When the gastrointestinal maladjustment remains unrelieved in spite of parental and professional care, developmental progress is severely handicapped. Vomiting may persist, colic may continue and infections of the respiratory tract may supervene. The developmental history of a child suffering from such disturbances is depicted in figure 10. Not only was epiphysial rating retarded, but weight, height and even psychomotor progress suffered. In a sense this was a protective measure, because the child obviously had not the resources required for vigorous growth. During convalescence amazing gains are often made and illustrate the resiliency of the constitution.

A somewhat similar pattern of progress is shown by children whose disability is expressed not in gastrointestinal maladjustment but in prematurity, as in the case of the child whose record appears in figure 11,

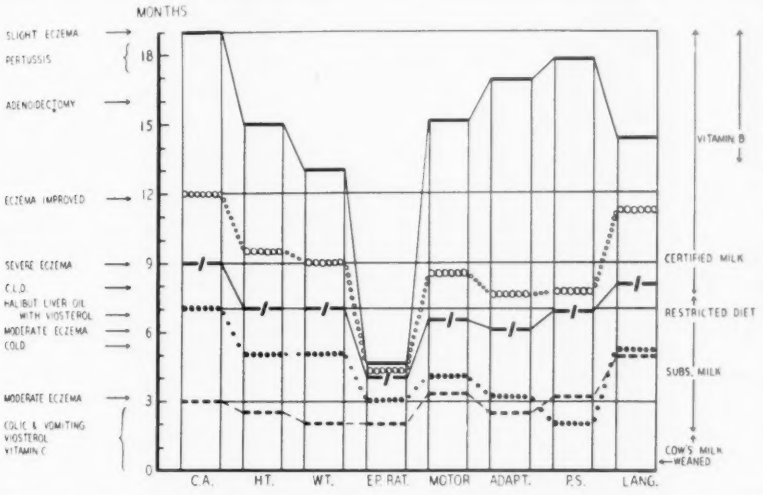

Fig. 10.—Chart of developmental progress of a white boy born June 14, 1933. The initial letters used as abreviations in the chart are to be interpreted as follows: C.L.O., cod liver oil; C.A., chronologic age; P.S., personal-social rating determined by the Gesell psychologic test as modified by Anderson.

assuming, of course, that there is no impairment of essential vital functions. Such children are small, though adequately nourished for their stature. Psychomotor progress usually remains within reasonable proximity to the standard. Stature and weight do not progress vigorously, but mineral resources are well built up, and the child is constitutionally healthy.

In the child whose record appears in figure 12 increase in stature was well maintained from birth. During the early months the inclusion of an ample vitamin D ration prevented the development of rickets, though it could not maintain adequate progress in epiphysial rating,

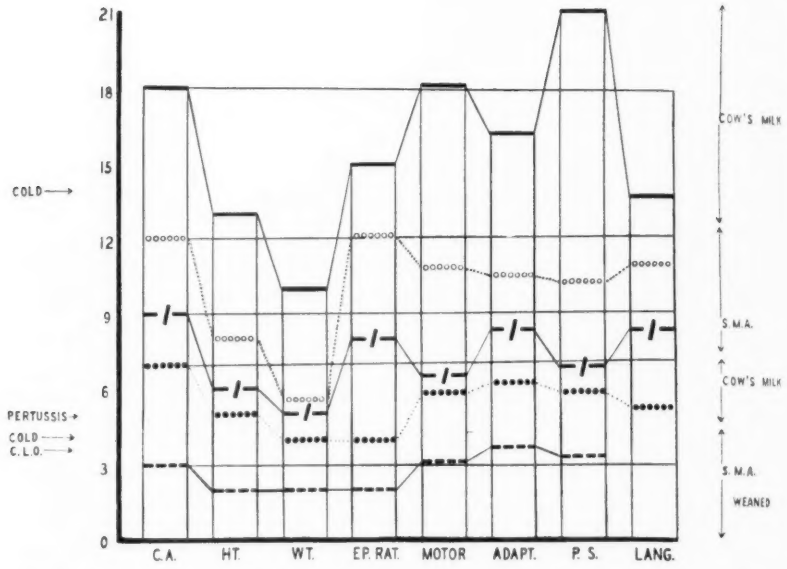

Fig. 11.—Chart of developmental progress of a white girl born Aug. 3, 1931. The initial letters used as abbreviations in the chart are to be interpreted as follows: C.L.O., cod liver oil; C.A., chronologic age; P.S., personal-social rating determined by the Gesell psychologic test as modified by Anderson; S.M.A., synthetic milk adapted.

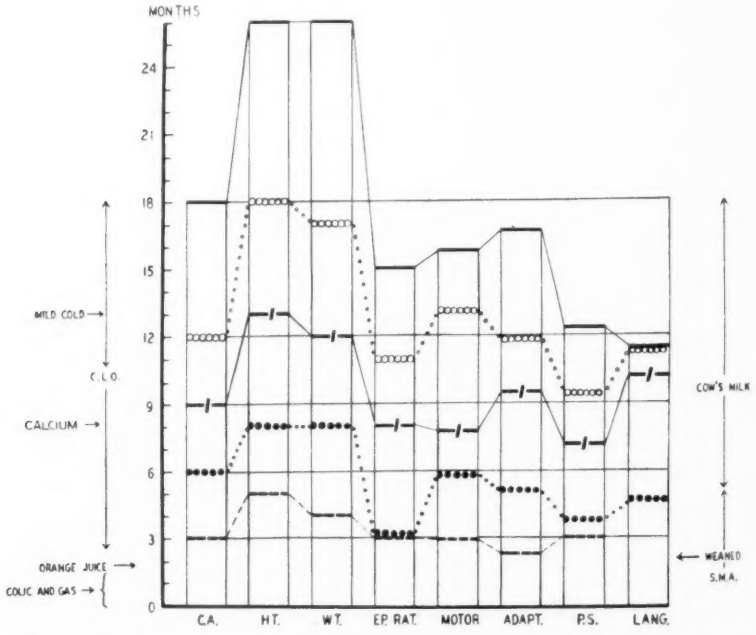

Fig. 12.—Chart of developmental progress of a white girl born Jan. 27, 1932. The initial letters used as abbreviations in the chart are to be interpreted as follows: C.L.O., cod liver oil; C.A., chronologic age; P.S., personal-social rating determined by the Gesell psychologic test as modified by Anderson; S.M.A., synthetic milk adapted.

owing to insufficiency of mineral in the diet for the demands of growth. The epiphysial rating promptly progressed when, at 8 months, the mineral ration was increased. This increase, however, was not maintained, because the demands of growth again took precedence in the utilization of available mineral.

The distinction in the effects of administration of vitamin D and of mineral has been clearly presented by Venar and Todd.[4] The inade-

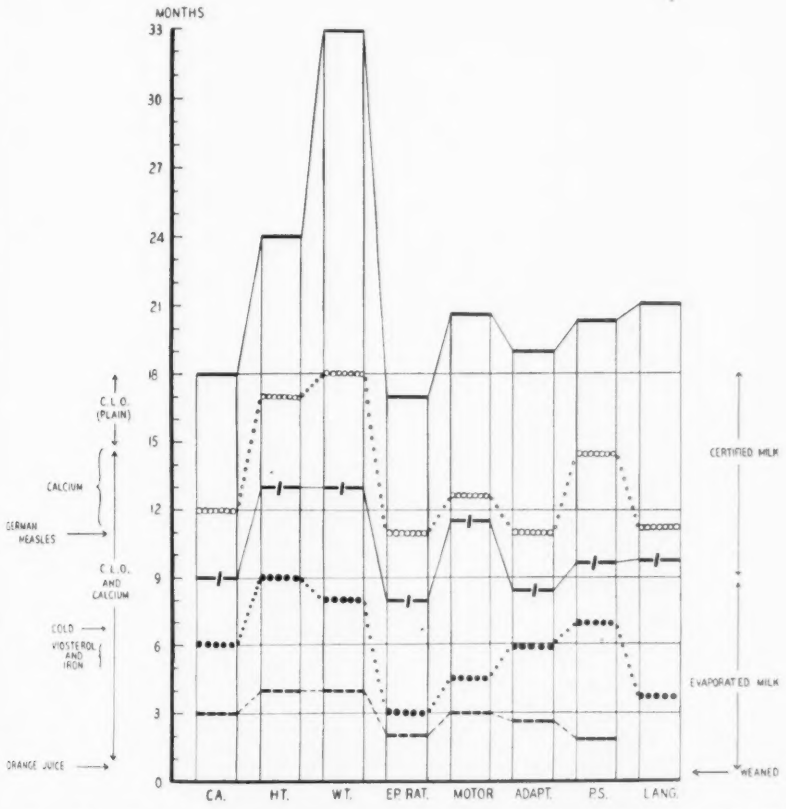

Fig. 13.—Chart of developmental progress of a white girl born June 9, 1932. The initial letters used as abbreviations in the chart are to be interpreted as follows: C.L.O., cod liver oil; C.A., chronologic age; P.S., personal-social rating determined by the Gesell psychologic test as modified by Anderson.

quacy of vitamin D to take the place of mineral in the diet has also been emphasized by Zucker,[5] who showed that in experimental animals the

4. Venar, Y., and Todd, T. W.: Experiments on the Maintenance of Mineral Density in the Skeleton, J. Lab. & Clin. Med. **22**:221-230, 1936.

5. Zucker, T. F.: Bone Ash in the Prevention and Healing of Experimental Rat Rickets, Science **84**:162-163, 1936.

normal level of 56 per cent ash in bones is easily reached provided an adequate mineral ration is available, whereas not more than 40 per cent ash can be attained by the administration of vitamin D in the absence of adequate mineral provision.

Figure 13 is the record of another child showing vigorous growth. During her first six months the diet was ample in mineral but low in vitamin D, so that on examination at the age of 6 months there was roentgen evidence of rickets. The prompt administration of larger doses of vitamin D corrected the lag in epiphysial rating, as was shown at subsequent examinations.

SUMMARY

1. There is a definite sequence as well as date of appearance for centers of ossification, but this schedule may be interrupted or retarded by metabolic or constitutional disturbance. Height, weight, bodily maturity and even mental expansion may show irregularities in progress.

2. Epiphysial rating is the earliest and frequently the only indicator of disturbance.

3. Progress in epiphysial rating may be used as a delicate measure of constitutional health in young children, but it will fail if employed as an indicator of bodily maturition.

4. Sick children show a lag in epiphysial rating proportionate to the duration and intensity of the constitutional disturbance. When convalescence is completed the epiphysial rating advances again.

5. Epiphysial rating is influenced by available mineral and vitamin D. Children on a low mineral ration tend to lag in epiphysial rating. As a corollary of this, children growing very rapidly will tend to lag in epiphysial rating unless they are provided with ample rations of mineral and of vitamin D. When the period of rapid growth comes to a close the epiphysial rating advances rapidly.

6. Children growing slowly and given a diet rich in mineral and vitamins, particularly vitamin D, tend to advance rapidly in epiphysial rating.

INTELLIGENCE RATING AND EMOTIONAL PATTERN OF ALLERGIC CHILDREN

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For many years it has been a popular conception that allergic persons possess superior mental traits, which for a time were considered to result directly from the allergic constitution. Balyeat,[1] in 1929, strongly supported the theory of the superior mental ability of the allergic person. He based his conclusions on the results of the Otis self-administering test, which was given to 80 allergic and 80 nonallergic children.

In 1937 Piness [2] and his associates made a similar study and reported their findings, which gave evidence that allergic children are similar in intelligence to normal children. Since these findings flatly contradicted those of Balyeat, we decided to study a group of allergic children in a similar manner, that we might secure further evidence on their mentality by comparing their intelligence quotients with those of the public school children of New York city. We also attempted to compare the emotional pattern and adjustability of the afflicted and of normal children. The children used in this study were obtained from the children's allergy clinic of the New York Post-Graduate Medical School and Hospital. Their educational status ranged from the beginning of kindergarten to the eighth grade of public school.

The ages of the children ranged from 5 years and 4 months to 15 years and 3 months. The median age for the group was 10 years and 11 months and the numerical age 10 years and 7 months, as shown in table 1. The total number of cases studied was 169.

Because of the differences in the ages of the children, different tests were used on each age group. The Pintner-Cunningham test was given to 35 children whose status ranged from kindergarten to the second grade. The Otis Primary Test was given to 19 children between the

From the allergy clinic of the pediatric department of the New York Post-Graduate Medical School and Hospital.

1. Balyeat, R. M.: The General Health and Mental Activity of Allergic Children, Am. J. Dis. Child. **37**:1193 (June) 1929.

2. Piness, G.; Miller, H., and Sullivan, E. B.: The Intelligence Rating of the Allergic Child, J. Allergy **8**:168 (Jan.) 1937.

second and the fourth grade. The National Intelligence Test was given to 57 children and the Pintner intelligence test to 38 children between the fourth and the eighth grade. The Stanford-Binet form M of the revised Binet scale was given to 20 children whose ages ranged from 2 years to 15 years and 3 months. The children to whom this Binet test was given were chosen at random from the whole experimental group. The tests are outlined in table 2, which shows the distribution of the intelligence quotients in the 169 cases studied.

TABLE 1.—*Age Distribution of Allergic Children*

Age Distribution	No. of Children
15 yr. - 15 yr. 11 mo.	2
14 yr. - 14 yr. 11 mo.	7
13 yr. - 13 yr. 11 mo.	12
12 yr. - 12 yr. 11 mo.	27
11 yr. - 11 yr. 11 mo.	32
10 yr. - 10 yr. 11 mo.	18
9 yr. - 9 yr. 11 mo.	19
8 yr. - 8 yr. 11 mo.	29
7 yr. - 7 yr. 11 mo.	18
6 yr. - 6 yr. 11 mo.	4
5 yr. - 5 yr. 11 mo.	1
Total	169

Median age, 10 yr. 11 mo.
Mean age, 10 yr. 7 mo.

TABLE 2.—*Difference in Intelligence Quotients with Different Tests*

Test	No. of Cases	Range in Intelligence Quotients	Median	Mean	Sigma	Probable Error
Pintner-Cunningham	35	88.20-107.70	98.50	98.20	13.60	9.27
Otis primary	19	101.70-119.30	113.50	111.10	15.10	10.19
National intelligence	57	85.70-118.20	102.20	103.70	16.20	10.92
Pintner intelligence	38	76.20-114.50	102.50	104.20	24.90	16.80
Binet	20	81.50-105.50	92.50	95.50	14.17	9.50
Total	169					
Average of four tests	149	88.25-117.75	102.30	103.50	19.75	13.32
Binet	20	81.50-105.50	92.50	95.50	14.17	9.55
Total	169					

The range of distribution of the quotients for the four tests was from 65 to 149, and included quotients of children whose status ranged from kindergarten to the last half of the eighth grade. The median quotient of the four tests was 102.3.

The individual Binet test showed a median of 92.5. This lower median was due to the selection of the children to whom it was administered. We found that of the 20 children we chose 7 proved to have intelligence below normal. This, together, with the fact that in this small number of cases the spread of the distribution was large, ranging from 68 to 119, lowered the median intelligence quotient. The mean quotient was 95.5.

On analysis of the types of tests passed and failed by the group as a whole, we found that allergic children show no direct evidence of specific proficiency or deficiency in any field of educational endeavor but that they vary in their abilities only according to their mental and educational status, just as any normal child does.

Table 3 represents the percentage distribution of the intelligence quotients of the allergic group as contrasted with that of a group from the schools of the city of New York.

The results indicate that the allergic group is neither retarded nor advanced as compared with a group of normal children. The slight difference between the median of the group from the schools of New

TABLE 3.—*Percentage Distribution of Intelligence Quotients of Allergic Group Contrasted with That of a Group from the Schools of New York City*

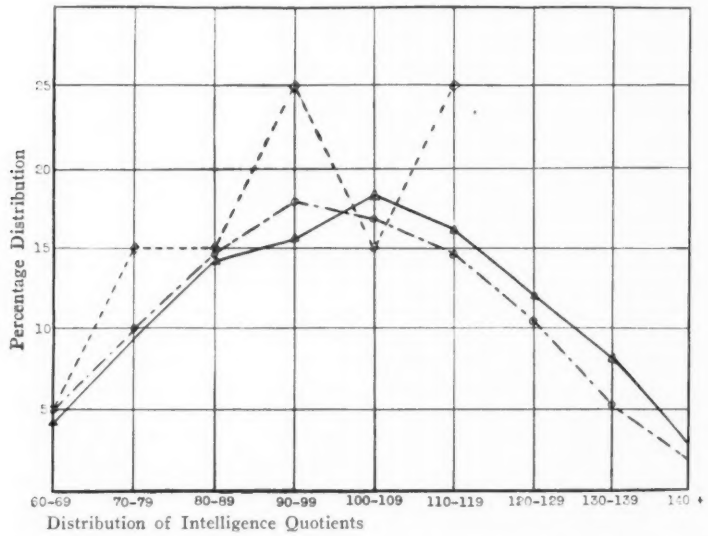
Intelligence Quotients, Distribution	Allergic Group		Group from Schools of New York: Group Intelligence Quotient Group Test, Percentage
	Stanford-Binet Intelligence Quotient, Percentage	Average of Four Intelligence Quotients, Percentage	
140-150	0	2.68	7.26
130-139	0	8.05	5.44
120-129	0	12.08	10.93
110-119	25	16.14	14.75
100-109	15	18.12	16.94
90- 99	25	15.43	17.55
80- 89	15	14.09	14.89
70- 79	15	9.39	9.86
60- 69	5	4.02	5.28
Below	0	0	0
Number of cases	20	149	100,000
Median	92.50	102.30	100.22
Mean	95.50	103.50	100.22
Sigma, standard deviation	14.17	19.75	20.87
Range of intelligence quotients	68-119	65-149	
Range of ages	7 yr - 13 yr. 4 mo.	5 yr. 4 mo. - 15 yr. 3 mo.	
Median age	10 yr. 11 mo.		
Numerical age	10 yr. 7 mo.		

York and that of the allergic group cannot be considered significant. The results also show that the group of allergic children range in mentality from inferior to superior intelligence. The percentage distribution of the intelligence quotients of the allergic group found in each level of intelligence agrees closely with the percentage present in each level of intelligence of the normal group from the schools of New York. This is demonstrated in the chart.

The results of our studies agree closely with the findings of Piness, showing that allergic children are similar in intelligence to normal ones and that they retain the same variations of inferior, normal and superior intelligence.

The second part of this paper is devoted to the presentation of the tentative results obtained from a study of the aspects of the personalities of allergic children.

An attempt was made to compare the personality of the allergic child with that of the normal child. This was done by using the Pintner Personality Outline, in which the subject is asked to compare his feelings toward a variety of statements (such as: "I am always sick," "I make believe I am some one else," "I do not like to be a leader in games," or "I would rather play with another child than alone") by encircling the word "same" or "different" to show his agreement or disagreement with the statement. This questionnaire is designed to measure (1) ascendency and submission, (2) extroversion and introversion and (3) emotional adjustment. In answering the questions the children were entirely free from any coaching or guidance.



A comparison of the intelligence quotients of allergic and of nonallergic groups of children. The unbroken line represents the composite curve of four tests; the line composed of equal dashes represents the standard curve of the schools of New York city and the line of unequal dashes represents the Binet curve.

The findings for a group of 20 girls are shown in table 4. They indicate that allergic girls are somewhat more stable emotionally and better adjusted to their environments than a similar group of nonallergic girls. However, the group is too small for a definite conclusion to be drawn. Table 5 reviews similar findings for a group of 45 boys.

In this group it seems that the boys are better adjusted to their environments than a normal, nonallergic group, but much less so than the group of allergic girls studied. The fact that the allergic girl is better adjusted and more stable emotionally than the allergic boy may be due to many factors. One may well be that parental suppression of

the physical activity of the allergic child causes resentments and conflicts to be built up because he is not allowed to pursue the activities of his playmates. Since a girl leads a less active play-life than a boy, such a factor would not be so telling in the cases of the allergic girl.

The evidence from the accumulated data is not sufficiently suggestive for one to determine definitely whether allergic children show more or less ascendency or extroversion than normal children. In this experimental group we found all degrees of submission and ascendency, the tendency being slightly toward submission and introversion for the group as a whole. It seems that the girls are more submissive than the boys. The variations, however, were so slight that no conclusive statement can be derived from the figures obtained thus far. As can be seen from the results of the extroversion and introversion tests, both the

TABLE 4.—*Comparison of Personalities of Normal and of Allergic Girls*

Test	Normal Girls, 1,000		Allergic Girls, 20	
	Median Score	Percentage	Median Score	Percentage
Ascendency and submission	16.5	50	17.0	55
Extroversion and introversion	23.0	50	22.0	45
Emotionality	29.0	50	30.5	61

TABLE 5.—*Comparison of Personalities of Normal and of Allergic Boys*

Test	Normal Boys, 1,000		Allergic Boys, 45	
	Median Score	Percentage	Median Score	Percentage
Ascendency and submission	17.5	50	19.0	60
Extroversion and introversion	23.0	50	22.6	43
Emotionality	28.0	50	28.8	54

allergic boys and the allergic girls were found to be slightly introverted. An attempt was then made to determine a composite picture of the attitude of the allergic children. To do this we used a Pupil's Portrait Questionnaire, compiled with norms by Dr. R. Pintner and his associates. The object of this questionnaire is the measurement of such attitudes as those of pupil to pupil, pupil to self and pupil to family. The children were asked to designate by encircling the words "same" or "different" how each statement applied to them as it stood in the questionnaire. The questions were of this type: "This child thinks only 'sissies' obey school rules"; "This child thinks the teacher is his friend"; "This child helps a classmate when he needs help"; "This child is glad when the teacher is absent," and "This child thinks he is a stranger at home."

The results are shown in table 6. The original norms were determined for 820 children in the schools of the city of New York. Our

results indicate that a normal girl rates higher in her adjustment to school, to the teacher, to the other pupils, to her family and to herself than an allergic girl, the total scores being 86.6 and 82.5, respectively.

This evidence seems contradictory to the previous statement that allergic girls are more stable than nonallergic girls; however, it is possible that this difference can be explained by the fact that the test on

TABLE 6.—*Results of Tests with Pupil's Portrait Questionnaire*

Type of Adjustment Tested	No. of Cases	Lower Quartile	Upper Quartile	Median	Mean	Sigma	Probable Error
Pupil-School							
Normal girls	387	13.33	15.34	14.65	14.09	1.73	
Normal boys	433	11.39	14.84	13.51	12.89	2.86	
Allergic girls	16	11.90	14.25	13.00	13.45	1.83	1.23
Allergic boys	40	10.78	14.88	12.70	12.52	2.44	1.61
Pupil-Teacher							
Normal girls	387	12.41	14.96	13.93	13.36	2.30	
Normal boys	433	9.80	14.31	12.63	11.77	3.35	
Allergic girls	16	11.00	13.38	12.50	12.68	2.30	1.54
Allergic boys	40	9.00	13.50	11.10	11.20	3.48	2.34
Pupil-Pupil							
Normal girls	387	16.14	18.89	17.70	17.12	2.57	
Normal boys	433	15.06	18.69	17.06	16.39	3.05	
Allergic girls	16	13.05	17.50	16.50	16.13	2.73	1.84
Allergic boys	40	14.16	17.87	16.15	15.95	3.27	2.20
Pupil-Self							
Normal girls	387	17.36	20.92	19.50	18.77	2.94	
Normal boys	433	15.84	19.63	18.97	17.95	3.65	
Allergic girls	16	16.16	19.00	18.25	18.37	1.53	1.03
Allergic boys	40	15.00	19.30	17.78	17.85	2.78	1.87
Pupil-Family							
Normal birls	387	21.59	25.55	23.87	23.04	3.77	
Normal boys	433	20.19	24.90	22.85	21.99	3.84	
Allergic girls	16	20.83	24.10	23.00	22.93	2.00	1.34
Allergic boys	40	18.50	22.90	20.90	20.92	3.15	2.12
School adjustment							
Normal girls	387	58.00	67.24	63.76	61.80	7.72	
Normal boys	433	52.64	65.44	60.48	57.60	10.52	
Allergic girls	16	56.50	62.00	59.50	59.50	5.83	3.93
Allergic boys	40	48.50	62.16	57.75	56.05	9.38	6.32
Total test score							
Normal girls	387	78.36	91.36	86.60	84.36	9.72	
Normal boys	433	72.56	89.68	83.08	79.48	13.64	
Allergic girls	16	80.50	84.50	82.50	82.30	6.32	4.86
Allergic boys	40	71.50	82.88	78.50	76.55	12.00	8.09
Pupil-School (average of boys' and girls' scores)							
Normal boys and girls	820	12.36	15.09	14.02	13.45	2.08	
Allergic boys and girls	56	11.07	13.97	12.71	12.97	2.28	1.53

aspects of personality measures adaptation to the total environment while the Pupil's Portrait Test is a more detailed analysis of adaptation to the various aspects of environment, showing particularly how the child reacts to a specific situation. This closer study of the child's attitudes toward environmental details discloses factors which bring out subtle signs of maladjustment. These might easily be overlooked in the consideration of the total environment.

The normal boy also showed a better adjustment than the allergic boy, the total scores being 83.3 and 78.5, respectively. The normal girl was better adjusted than the normal boy, as indicated by a total score of 86.6 to 83.08, and the allergic girl showed a better adjustment than the allergic boy by a total score of 82.5 to 78.5. Thus it can be seen that the nonallergic boy and girl have a better attitude than their allergic schoolmates.

CONCLUSIONS

Results of this study agree closely with the findings of Piness.

Allergic children are neither retarded nor advanced in intelligence as compared with normal children.

The distribution of the intelligence scores of allergic children closely follows the normal curve, showing variations of inferior, normal and superior intelligence to the same degree as that of normal children.

Allergic children show no evidence of specific proficiency or deficiency in any field of educational endeavor. They vary in their abilities only according to their mental and educational status, just as any normal child does.

Allergic girls are emotionally more stable and better adjusted to their environment than allergic boys.

Allergic children show all degrees of ascendency and submission, extroversion and introversion, the tendency being slightly toward submission and introversion for the group as a whole.

BASAL METABOLISM AND PREFORMED AND TOTAL CREATININE IN URINE OF SEVENTY CHILDREN

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In view of the growing interest in the relation between basal metabolism and the urinary output of preformed and total creatinine, the present report was prepared from the values which have appeared in previous publications by my co-workers and me, supplemented by our unpublished data. As early as 1914 Palmer and his collaborators [1] pointed out the possibility of using urinary creatinine as a basis for the evaluation of basal metabolism. In a study conducted on 31 men and 21 women Takahira [2] found that the urinary creatinine was proportional not only to body weight but to the basal metabolism as well. Guhr [3] also demonstrated a definite relation between excretion of creatinine and basal metabolism in his patients with thyroid disease. However, the author pointed out that this relationship did not exist in patients treated with either roentgen rays or radium. In cases of exophthalmic goiter Eimer [4] failed to find a close correlation between creatinine output and basal metabolism. More recently Talbot [5] demonstrated a close relation between creatinine excretion and basal metabolism in a study conducted on 15 children between the ages of 7 and 15 years, of whom 3 were classed as physically normal while the majority were patients from the neurologic ward. In conclusion, the author stated:

A method for the evaluation of measurements of basal energy metabolism devised on the basis of the excretion of creatinine for twenty-four hours is probably more accurately informative than the existing standards of reference.

The experimental work reported in this paper was conducted in part at the Children's Hospital Research Foundation, Cincinnati, and in part at the Nelson Morris Memorial Institute for Medical Research of the Michael Reese Hospital, Chicago.

1. Palmer, W. W.; Means, J., and Gamble, J. L.: Basal Metabolism and Creatinine Elimination, J. Biol. Chem. **19**:239 (Aug.) 1914.

2. Takahira, H.: Parallélisme entre l'excrétion de la créatinine et le métabolisme de base, Bull. Soc. scient. d'hyg. aliment. **15**:492, 1927.

3. Guhr, M.: Creatinine in the Urine as an Index of Degree of Basal Metabolism, West. J. Surg. **39**:921 (Dec.) 1931.

4. Eimer, K.: Beziehungen der Kreatin Körperausscheidung zu Stoffwechsel und Schilddrüsenfunktion, Ztschr. f. d. ges. exper. Med. **77**:455, 1931.

5. Talbot, N. B.: Basal Energy Metabolism and Creatinine in the Urine: I. Observations of Children, Am. J. Dis. Child. **52**:16 (July) 1936.

The data in this report consist of the values for basal metabolism and for the urinary output of preformed and total creatinine nitrogen of 24 boys between the ages of 5 weeks and 13 years and of 46 girls from 4 to 15 years of age. All the boys except 1, who had reached his thirteenth birthday, were under 10 years of age, and only 5 girls had reached puberty. Fifty-five per cent of the children were within a 10 per cent deviation from the height-weight standard of Baldwin and Wood. With the exception of 1, who was 12 per cent overweight, all were underweight, with a maximum deviation of 26 per cent. Otherwise, all the children appeared normal on medical examination.

EXPERIMENTAL METHODS

The general procedure and the technic of feeding and of collection and analysis of specimens of urine of the children over 1 year of age have been described in our previous communications.[6] In the case of infants, a metabolism bassinet was employed for collecting twenty-four hour specimens of urine in our early work. Later the bassinet was replaced by a hammock, which could be laundered more easily. For basal metabolic determinations either the Benedict cot chamber in connection with the universal respiration apparatus[7] or the open circuit method in Higgins' modification[8] of the Benedict cot chamber was employed for children under 6 years of age. When the latter method was used the expired air was analyzed in a Carpenter-Haldane apparatus for gas analysis. The basal metabolic rates of the older children were determined by the open circuit method, as described in our previous papers.[9]

The averages of twenty-four hour values for six day outputs of preformed and of total creatinine nitrogen[10] and of basal metabolism expressed in terms of both total calories per twenty-four hours and calories per milligram of preformed and of total creatinine nitrogen output (i. e., the ratio of the basal metabolic rate to the preformed and the total creatinine nitrogen excreted) were grouped according to and correlated with age, weight, height and surface area. The values for basal metabolism were also grouped according to the twenty-four hour output of

6. (*a*) Wang, C. C.; Frank, M.; Hays, B. B., and Kern, R.: Metabolism of Undernourished Children: I. Gain in Weight, Am. J. Dis. Child. **32**:63 (July) 1926; (*b*) III. Urinary Nitrogen with Special Reference to Creatinine, ibid. **32**: 360 (Sept.) 1926. (*c*) Wang, C. C.; Kaucher, M., and Wing, M.: Metabolism of Adolescent Girls: I. Basal Metabolism and Energy Exchange, ibid. **51**:801 (April) 1936. (*d*) Wang, C. C.; Genther, I., and Hogden, C.: III. The Excretion of Creatinine and Creatine, ibid. **51**:1268 (June) 1936.

7. Benedict, F. G., and Tompkins, E. H.: Respiratory Exchange, with a Description of a Respiration Apparatus for Clinical Use, Boston M. & S. J. **174**: 857 (June 15); 898 (June 22); 939 (June 29) 1916.

8. Higgins, H. L., and Bates, V.: New Method for the Determination of the Basal Metabolism of Babies and of Small Children, Am. J. Dis. Child. **39**:71 (Jan.) 1930.

9. Wang, C. C.; Kern, R.; Frank, M., and Hays, B. B.: Metabolism of Undernourished Children: II. Basal Metabolism, Am. J. Dis. Child. **32**:350 (Sept.) 1926. Wang, Kaucher and Wing.[6c]

10. The values of total creatinine nitrogen were obtained for 53 children.

TABLE 1.—*Values of Basal Metabolism and of Urinary Preformed and Total Creatinine Nitrogen for Seventy Children*

Subject	Sex	Age, Years	Height, Cm.	Weight		Surface Area, Sq. Meters	Preformed Creatinine Nitrogen, Mg.		Total Creatinine Nitrogen, Mg.		Basal Metabolism, Calories		Calories per Mg. of Preformed Creatinine Nitrogen	Calories per Mg. of Total Creatinine Nitrogen
				Observed, Kg.	Deviation from Standard, Percentage		Per Day	Per Kg. per Day	Per Day	Per Kg. per Day	Per Day	Per Kg. per Day		
1	M	0.13	53	3.88	− 5.8	0.227	18.2	4.7	21.0	5.4	207	53.4	11.37	9.86
2	M	0.21	59	4.93	− 8.5	0.272	24.7	5.0	39.4	8.0	299	60.7	12.11	7.59
3	M	0.27	61	5.21	−10.7	0.285	26.1	5.0	35.9	6.9	276	53.1	10.57	7.69
4	M	0.31	63	5.54	−11.8	0.300	26.6	4.8	53.7	9.7	301	54.4	11.32	5.61
5	M	0.40	65	6.01	−16.1	0.318	28.8	4.8	49.3	8.2	348	57.2	12.08	7.06
6	M	0.42	66	6.22	−15.7	0.326	32.3	5.2	59.1	9.5	345	55.5	10.68	5.84
7	M	0.45	66	6.47	−14.7	0.331	29.1	4.5	44.0	6.8	381	58.9	13.09	8.66
8	M	0.42	65	6.13	−12.9	0.320	29.4	4.8	49.7	8.1	337	55.0	11.46	6.78
9	M	0.54	67	7.50	− 4.3	0.357	30.8	4.1	45.0	6.0	430	57.3	13.96	9.56
10	M	0.71	70	8.80	+ 4.7	0.394	40.5	4.6	69.5	7.9	518	58.8	12.79	7.45
11	M	0.92	75	10.03	+ 2.8	0.438	46.1	4.6	97.3	9.7	537	54.0	11.65	5.52
12	M	5	95	14.5	+ 0.4	0.608	103	7.1	128	8.8	870	60	8.45	6.80
13	M	7	106	15.2	−11.4	0.671	137	9.0	210	13.8	1,049	69	7.66	5.00
14	M	6	108	16.4	− 7.6	0.703	118	7.2	190	11.7	968	59	8.20	5.09
15	M	7	106	16.9	− 1.5	0.702	139	8.2	230	13.6	862	51	6.20	3.75
16	F	4	105	17.0	+ 0.6	0.699	107	6.3	...	....	816	48	7.63	....
17	F	6	116	17.0	−16.4	0.752	102	6.0	...	....	884	52	8.67	....
18	M	6	108	17.2	− 2.8	0.717	122	7.1	...	....	1,015	59	8.32	....
19	F	6	115	17.2	−14.9	0.751	143	8.3	237	13.8	929	54	6.50	3.92
20	F	6	108	17.3	− 4.2	0.719	116	6.7	163	9.4	969	56	8.35	5.94
21	F	7	116	17.3	−16.0	0.757	138	8.0	199	11.5	952	55	6.90	4.78
22	M	7	116	17.9	−11.8	0.769	136	7.6	204	11.4	859	48	6.32	4.21
23	F	5	108	18.0	+ 1.2	0.731	117	6.5	...	....	990	55	8.46	....
24	F	6	115	18.0	−11.3	0.765	144	8.0	225	12.5	900	50	6.25	4.00
25	F	6	109	18.1	− 0.8	0.738	127	7.0	194	10.7	977	54	7.69	5.04
26	F	6	115	18.6	− 8.4	0.776	136	7.3	192	10.3	874	47	6.43	4.55
27	F	6	117	18.8	−10.3	0.789	117	6.2	...	....	884	47	7.56	....
28	F	7	120	18.8	−15.0	0.804	135	7.2	...	....	940	50	6.96	....
29	F	8	125	19.1	−24.3	0.833	139	7.3	...	....	840	44	6.04	....
30	F	10	132	20.8	−24.7	0.899	164	7.9	...	....	915	44	5.58	....
31	F	8	118	21.0	− 3.0	0.833	162	7.7	...	....	819	39	5.06	....

32	F	9	125	21.8	— 9.8	0.882	187	8.6	207	9.5	1,025	47	5.48	4.95
33	M	8	123	22.3	— 5.9	0.880	178	8.0	202	13.1	1,137	51	6.39	3.89
34	F	10	133	22.9	—23.2	0.942	167	7.3	...	....	1,008	44	6.04	....
35	M	8	124	23.1	— 3.2	0.899	155	6.7	...	....	1,155	50	7.45	....
36	M	10	128	23.7	— 8.9	0.929	201	8.5	273	11.5	1,114	47	5.54	4.08
37	F	9	123	23.9	+ 2.9	0.907	203	8.5	263	11.0	1,052	44	5.18	4.00
38	M	10	131	25.4	— 6.8	0.974	163	6.4	224	8.8	1,016	40	6.23	4.54
39	M	10	137	25.5	—16.4	1.008	230	9.0	273	10.7	1,071	42	4.66	3.92
40	F	9	132	27.0	— 4.4	1.005	232	8.6	297	11.0	999	37	4.31	3.36
41	F	10	134	27.1	— 8.0	1.017	192	7.1	...	....	1,111	41	5.79	....
42	F	10	133	27.3	— 5.2	1.015	191	7.0	...	....	983	36	5.15	....
43	F	10	132	27.5	— 2.5	1.009	209	7.6	...	....	1,128	41	5.40	....
44	F	10	134	27.6	— 6.3	1.025	221	8.0	...	....	1,021	37	4.62	....
45	M	10	137	27.6	— 9.7	1.042	257	9.3	348	12.6	1,049	38	4.08	3.01
46	F	14	138	27.8	—18.8	1.049	247	8.9	442	15.9	968	35	3.92	2.19
47	M	13	138	27.9	—11.0	1.052	240	8.6	299	10.7	1,228	44	5.12	4.11
48	F	12	137	29.0	— 7.3	1.062	237	8.1	290	10.0	1,044	36	4.83	3.60
49	F	12	140	30.5	— 7.6	1.102	285	9.3	445	14.6	1,074	35	3.77	2.41
50	F	13	147	30.6	—22.5	1.145	277	9.0	477	15.6	1,144	38	4.13	2.40
51	F	11	138	30.9	— 2.8	1.090	241	7.8	...	....	1,082	35	4.49	....
52	F	13	148	32.7	—18.3	1.186	289	8.8	419	12.8	1,090	33	3.77	2.60
53	F	12	147	32.9	—14.0	1.181	278	8.4	461	14.0	1,204	37	4.33	2.61
54	F	11	140	34.7	+ 6.0	1.166	208	6.0	...	....	1,284	37	6.17	....
55	F	13	146	35.6	— 7.7	1.217	287	7.6	456	12.8	1,242	35	4.33	2.72
56	F	12	151	36.2	—13.1	1.256	315	8.7	496	13.7	1,138	31	3.61	2.29
57	F	12	157	36.2	—22.9	1.290	290	8.0	434	12.0	1,273	35	4.39	2.93
58	F	14	154	37.0	—22.5	1.282	284	7.6	437	11.8	1,193	33	4.20	2.73
59	F	13	161	37.2	—26.0	1.328	307	8.3	454	12.2	1,316	35	4.29	2.90
60	F	13	157	38.8	—18.4	1.330	340	8.7	532	13.7	1,285	33	3.78	2.42
61	F	15	157	40.3	—20.1	1.350	373	9.3	520	12.9	1,271	32	3.41	2.44
62	F	12	144	40.5	+12.4	1.273	317	7.8	540	13.3	1,211	30	3.82	2.24
63	F	12	151	41.3	— 0.5	1.324	372	9.0	512	12.4	1,242	30	3.34	2.43
64	F	12	154	41.9	— 5.6	1.354	350	8.4	499	11.9	1,262	30	3.61	2.73
65	F	15	154	43.8	—10.0	1.380	395	9.0	491	11.2	1,184	27	3.00	2.41
66	F	13	167	43.9	—21.8	1.467	334	7.6	483	11.0	1,362	31	4.08	2.82
67	F	13	163	46.5	—13.4	1.463	414	8.7	512	11.0	1,300	29	3.14	2.54
68	F	14	167	46.9	—15.7	1.504	383	8.2	586	12.5	1,429	31	3.73	2.44
69	F	15	165	50.9	— 5.5	1.543	452	8.9	611	12.0	1,460	29	3.23	2.39
70	F	15	162	52.9	— 1.1	1.551	385	7.3	455	8.6	1,382	26	3.59	3.04

preformed creatinine nitrogen and were correlated with values for both the preformed and the total creatinine nitrogen. The results are given in tables 1 to 5 and in charts 1 and 2.

INFLUENCE OF AGE, WEIGHT, HEIGHT AND SURFACE AREA ON BASAL METABOLIC RATE, ON CREATININE OUTPUT AND ON THE RATIO OF THE TWO AND INFLUENCE OF PREFORMED CREATININE NITROGEN OUTPUT ON BASAL METABOLIC RATE

Table 2 and charts 1 and 2 give the results of the averages grouped according to age, weight, height, surface area and urinary output of preformed creatinine nitrogen. Owing to the similarity of the courses followed by the different groups, only the curves for the basal metabolic rates and the preformed creatinine nitrogen output of the age group and the curve for the ratio of the two factors of the creatinine group are given here. With the exception of the number of calories per milligram of preformed and of total creatinine nitrogen, the total twenty-four hour values of all factors increased steadily and rapidly with the rise of age, weight, height, surface area and urinary creatinine nitrogen output. But the rate of increase of the various factors at different ages was not always similar. Under the age of 5 years, especially during the first year of life, the level of the basal metabolism augmented much more rapidly than that of the preformed creatinine nitrogen (chart 1). Consequently, the two curves crossed each other during the first year. From the age of 5 to that of 11 years the increase of creatinine output exceeded that of the basal metabolic rate. This was followed by a period of three years when the two curves ran nearly parallel. During the year between the age of 14 and that of 15 years the creatinine output increased much more rapidly than the basal metabolic rate. Since the diet was controlled and no medication was employed, it is difficult to explain the difference in the speed of rise unless it is possible that, aside from active protoplasmic tissue, another factor or factors is responsible for the production of either heat or creatinine or both. In their recent paper Talbot and his associates [11] also noted that many accessory factors may modify the amount of heat produced, even under basal conditions. These authors stated: "Age, for example, seems to have some effect, and different eras of life are physiologically unlike."

Furthermore, working on adult animals (varying from mice to elephants) with weights from 0.02 to 4,000 Kg., Brody and his asso-

11. Talbot, F. B.; Wilson, E. B., and Worcester, J.: Basal Metabolism of Girls, Am. J. Dis. Child. **53**:275 (Jan.) 1937.

ciates [12] mentioned that the basal metabolic rate and the preformed creatinine output were not directly proportional. Ashworth and Brody [13] and Smuts [14] also pointed out that the basal metabolic rate and the total urinary endogenous nitrogen content, but not the creatinine content, were directly proportional and that the ratio of the two was a constant, whereas the ratio of the basal metabolic rate to the creatinine value decreased with the increase of weight of the animal.[15]

When the results were expressed in terms of calories per kilogram of body weight, the curves were entirely different. The basal metabolic rate was highest during the second half of the first year, and then declined slowly for about seven years. The decrease became more rapid during the next four years, and then the curve became a flat line, followed by another rapid decline during the ages of 14 and 15 years. The level of preformed creatinine nitrogen, on the other hand, increased steadily and rapidly from a minimum average of 4.6 mg. per kilogram during the second six months of life to a value of 8 mg. at about the age of 10 years. Thereafter the rate of increase declined, and the value approached the figure for an adult. These changes were more clearly demonstrated by the groups divided according to weight, height, surface area and excretion of preformed creatinine (table 2). Here, again, the level of preformed creatinine followed an entirely different course from that of heat production, and the possibility of the existence of another factor responsible for either production of creatinine or basal metabolic rate is supported. The value for total creatinine nitrogen

12. Brody, S.; Procter, R. C., and Ashworth, U. S.: Growth and Development: XXXIV. Basal Metabolism, Endogenous Nitrogen, Creatinine and Neutral Sulphur Excretions as Functions of Body Weight, Bulletin 220, University of Missouri, College of Agriculture, Agricultural Experiment Station, 1934.

13. Ashworth, U. S., and Brody, S.: Growth and Development: XXVIII. Decline of Endogenous Nitrogen Excretion per Unit Weight with Increasing Weight in Growing Rats, and Its Relation to the Decline in Basal Metabolism: Decline in Live Weight, Nitrogen and Energy Metabolism with the Advance of the Period of Nitrogen Starvation and the Influence of Live Weight and of Preceding Level of Protein Intake on These Declines and on the Survival Periods, Bulletin 190, University of Missouri, College of Agriculture, Agricultural Experiment Station, 1933.

14. Smuts, D. B.: The Relation Between the Basal Metabolism and the Endogenous Nitrogen Metabolism, with Particular Reference to the Estimation of the Maintenance Requirement of Protein, J. Nutrition **9**:403 (April) 1935.

15. Ashworth, U. S., and Brody, S.: Growth and Development: XXVII. Endogenous Urinary Nitrogen and Total Creatinine Excretion in Rats as Functions of Dietary Protein Level, Time on N-Free Diets, Age, Body Weight and Basal Metabolism, Bulletin 189, University of Missouri, College of Agriculture, Agricultural Experiment Station, 1933; XXIX. Age Curves of Creatinine and Urinary Nitrogen Coefficients in Dairy Cattle, and Their Relations to Energy Metabolism, Bulletin 191, ibid., 1933.

also increased with growth, but it began to decline between the ages of 11 and 12 years. This was undoubtedly due to the decrease in creatine excretion of the children at that age.

The basal metabolic rate expressed in terms of calories per milligram of preformed creatinine nitrogen output was likewise highest

TABLE 2.—*Average Values of Creatinine Nitrogen and of Basal Metabolism Grouped According to Age, Weight, Height and Surface Area*

		Creatinine Nitrogen, Mg.				Basal Metabolism			
		Preformed		Total					
	No. of Subjects	Total per 24 Hr.	Per Kg. per 24 Hr.	Total per 24 Hr.	Per Kg. per 24 Hr.	Total Calories per 24 Hr.	Calories per Kg. per 24 Hr.	Calories per Mg. of Preformed Creatinine Nitrogen	Calories per Mg. of Total Creatinine Nitrogen
Age, Yr.									
0.13-0.4	5	25	4.9	40	7.6	286	56	11.49	7.56
0.42-0.92	6	35	4.6	61	8.0	425	57	12.27	7.30
4-6	12	121	7.0	190	11.0	923	53	7.71	5.05
7-8	9	147	7.7	227	12.7	957	51	6.55	4.33
9-10	13	201	8.0	269	10.7	1,038	41	5.24	3.98
11-12	10	289	8.2	460	12.9	1,181	34	4.24	2.63
13-15	15	334	8.4	478	12.3	1,257	33	3.85	2.68
Weight, Kg.									
3-6	4	24	4.9	38	7.5	271	55	11.34	7.69
6.1-10	7	34	4.7	59	8.0	414	57	12.24	7.27
13-15	2	120	8.1	169	11.3	960	65	8.06	5.90
16-20	16	127	7.2	204	11.7	916	52	7.28	4.69
21-25	9	176	7.7	252	10.8	1,027	45	5.88	4.23
26-30	10	226	8.2	325	11.8	1,060	39	4.79	3.01
31-35	6	263	8.2	451	14.3	1,146	36	4.44	2.64
36-40	6	304	8.2	468	12.7	1,241	34	4.10	2.56
41-45	6	357	8.5	508	12.1	1,255	30	3.54	2.55
46-56	4	409	8.5	541	11.3	1,393	29	3.42	2.60
Height, Cm.									
53-65	5	25	4.9	40	7.6	286	56	11.49	7.56
66-75	6	35	4.6	61	8.0	425	57	12.27	7.30
95-110	9	121	7.2	185	11.3	946	57	7.88	5.27
111-120	9	135	7.4	211	11.9	893	49	6.74	4.29
121-130	6	177	7.9	259	11.3	1,054	47	6.01	4.23
131-140	16	218	7.9	327	11.8	1,061	39	5.01	3.39
141-150	5	290	8.3	471	13.7	1,178	35	4.08	2.54
151-160	8	340	8.6	490	12.5	1,231	31	3.67	2.53
161-170	6	379	8.2	517	11.2	1,375	30	3.68	2.69
Surface Area, Sq. M.									
0.200-0.300	4	24	4.9	38	7.5	271	55	11.34	7.69
0.301-0.450	7	34	4.7	59	8.0	414	57	12.24	7.27
0.601-0.750	9	121	7.3	186	11.3	946	57	7.88	5.27
0.751-0.900	14	145	7.5	222	11.7	937	48	6.54	4.33
0.901-1.050	12	209	8.0	303	11.6	1,043	40	5.08	3.59
1.051-1.200	8	257	8.3	399	13.0	1,144	37	4.58	2.96
1.201-1.350	9	321	8.3	487	12.8	1,241	33	3.91	2.58
1.351-1.550	7	388	8.3	520	11.0	1,340	29	3.48	2.60

during the second half of the first year of life. It then declined rapidly throughout childhood, as was observed by previous investigators[15] in animal experiments. When the values were grouped according to the twenty-four hour output of preformed creatinine nitrogen, the group averages formed a smooth curve (chart 2). Except for the results with children under 1 year of age, my values, in agreement with Talbot's,[5] lie closer to this curve than to curves based on age, weight, height or surface area.

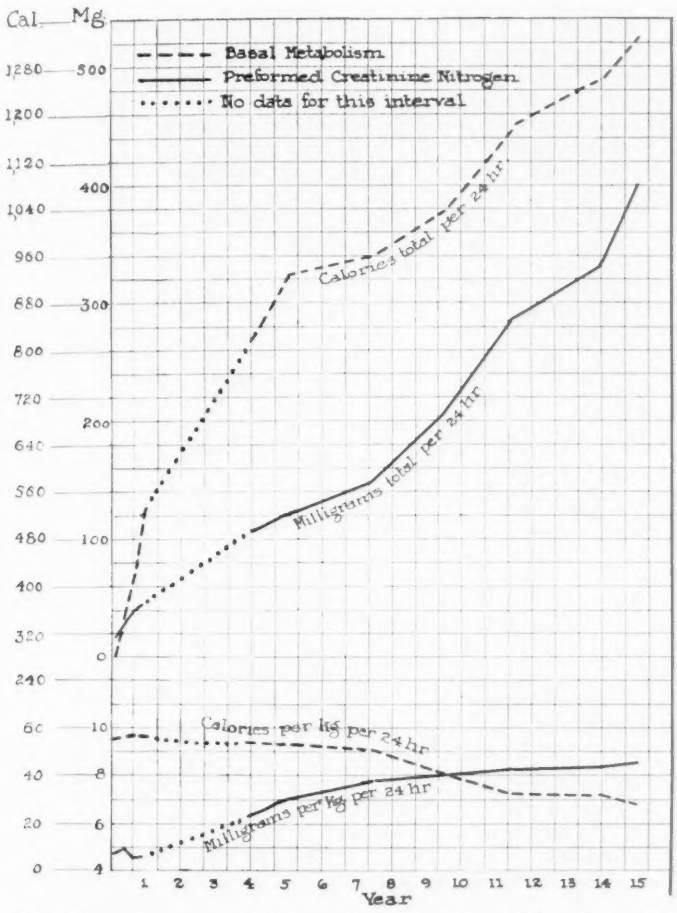

Chart 1.—Group averages of basal metabolic rates and of preformed creatinine nitrogen output for 70 children.

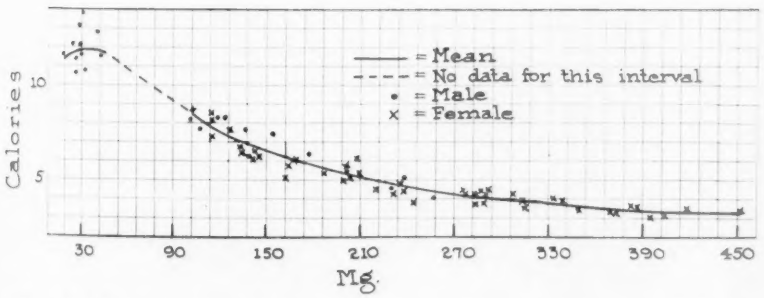

Chart 2.—Ratio of basal metabolic rate to preformed creatinine nitrogen referred to total preformed creatinine nitrogen per twenty-four hours.

COMPARISON OF THE RELATION OF VARIOUS FACTORS ACCORDING TO THEIR COEFFICIENTS OF CORRELATION

Is preformed creatinine output more closely correlated with heat production than with other factors? In order to answer this question, the twenty-four hour values for preformed creatinine nitrogen and for basal metabolism were correlated with each other and with various other factors, i. e., age, weight, height, surface area and total creatinine nitrogen output. Table 3 shows that all the coefficients of correlation were

TABLE 3.—*Coefficients of Correlation*

I. Preformed creatinine nitrogen to,	
1. Height	+0.938 ± 0.010
2. Weight	+0.981 ± 0.003
3. Surface area	+0.974 ± 0.004
4. Age	+0.939 ± 0.010
5. Basal metabolism (total calories per 24 hours)	+0.879 ± 0.018
6. Basal metabolism (calories per mg. of preformed creatinine nitrogen)	+0.923 ± 0.012
II. Total creatinine nitrogen to	
1. Height	+0.948 ± 0.009
2. Weight	+0.963 ± 0.007
3. Surface area	+0.968 ± 0.006
4. Age	+0.942 ± 0.010
5. Basal metabolism (total calories per 24 hours)	+0.899 ± 0.018
III. Basal metabolism (total calories per 24 hours) to	
1. Height	+0.956 ± 0.007
2. Weight	+0.899 ± 0.015
3. Surface area	+0.937 ± 0.010
4. Age	+0.922 ± 0.012
IV. Basal metabolism (calories per mg. of preformed creatinine nitrogen) to	
1. Height	−0.948 ± 0.008
2. Weight	−0.974 ± 0.004
3. Surface area	−0.920 ± 0.012
4. Age	−0.964 ± 0.006
V. Basal metabolism (calories per mg. of total creatinine nitrogen) to	
1. Height	−0.916 ± 0.013
2. Weight	−0.856 ± 0.025
3. Surface area	−0.889 ± 0.019
4. Age	−0.901 ± 0.017

exceptionally high and, aside from those concerned with basal metabolism, expressed in calories per milligram of preformed and total creatinine nitrogen excreted, were all positive. Preformed creatinine nitrogen levels were most closely correlated with body weight, with a value of + 0.981, and, contrary to expectation, least closely with basal metabolism expressed in terms of total calories per twenty-four hours, with a value of + 0.879. Instead of body weight or preformed creatinine nitrogen content, basal metabolism was most closely correlated with height, with a coefficient of + 0.956, which shows that in this group of children the preformed creatinine was more closely related to the mass of active protoplasmic tissue than to the basal metabolism. These find-

ings are not strictly in accordance with some reported in the literature. The difference between my various coefficients, however, was not significant and may easily have been the result of the large number of underweight children included in this study.

Unlike the total number of calories per twenty-four hours, basal metabolism expressed in terms of calories per milligram of preformed creatinine nitrogen excreted was correlated most closely with weight, with a coefficient of —0.974, which shows that the relation between preformed creatinine output and the mass of muscle tissue is probably closer than that between the creatinine output and other factors. Its lowest coefficient, —0.92, expressed the correlation with surface area.

TABLE 4.—*Comparison of Values Obtained for Boys and for Girls*

	Preformed Creatinine Nitrogen, Mg.				Total Creatinine Nitrogen, Mg.			
	Total per Day		Per Kg. per Day		Total per Day		Per Kg. per Day	
Age, Years	M	F	M	F	M	F	M	F
5	107	117	7.1	6.5				
6	126	126	7.2	7.1	190	202	11.7	11.2
7	137	137	8.3	7.6	215	199	12.9	11.5
8	167	151	7.4	7.5				
10	213	191	8.3	7.5				
13	240	321	8.6	8.4	299	476	10.7	12.7

	Basal Metabolism							
	Total Calories per 24 Hr.				Calories per Mg. of			
	Total per Day		Per Kg. per Day		Preformed Creatinine Nitrogen		Total Creatinine Nitrogen	
Age, Years	M	F	M	F	M	F	M	F
5	870	990	66	55	8.45	8.46		
6	990	917	59	51	8.26	7.35	5.09	4.69
7	923	946	56	53	6.73	6.93	4.32	4.78
8	1,146	830	51	42	6.92	5.55		
10	1,063	1,028	42	41	5.13	5.43		
13	1,228	1,248	44	33	5.12	3.93	4.11	2.63

The coefficients of correlation obtained between calories per milligram of total creatinine nitrogen excreted and the other factors ranged from —0.916 to —0.856. They were all lower than the corresponding values obtained from correlation with calories per milligram of preformed creatinine nitrogen, which indicates the possibility of exogenous influence on the excretion of creatine.

INFLUENCE OF SEX

Table 4 compares the values for the two sexes at different ages during growth. With the exception of the 13 year old group, in which the values for preformed and for total creatinine nitrogen were markedly higher for girls, sex had little influence on twenty-four hour values for either basal metabolism or creatinine nitrogen. Both increased with the growth of the children. Differing from values for total calories

per twenty-four hours, the per kilogram values for the basal metabolism of boys were invariably higher than those of girls. In spite of the slightly higher value for the girls in the 13 year old group, their per kilogram value was much lower than that for the boys, which showed that during this period the girls gained more in weight (probably in the form of inert tissues) than the boys. The level of preformed creatinine nitrogen, also, was higher for boys in three of the six groups and was comparable in others. The total creatinine nitrogen output of the boys was slightly higher in two groups and markedly lower in the 13 year old group; this probably resulted from the decreased excretion of creatine of boys during this prepubertal period.

Values for basal metabolism expressed in terms of calories per milligram of preformed and total creatinine nitrogen excreted showed little difference between the two sexes, except that the value for the 13 year old group of the girls was much lower than that for the boys and was closer to the adult value of 2.87 calories which I obtained previously for 6 normal women.

COMMENT

In part, the findings in the present communication agreed with those reported in the literature,[16] which demonstrated that there was a relationship between basal metabolism and the preformed creatinine in the urine and that it might be possible to employ the values of the latter as a basis for the evaluation of basal metabolism. With the exception of Talbot,[5] all the previous investigators dealt with adults only. None of the authors compared the variation of body weight with that of the ratio of the basal metabolic rate to the level of urinary preformed creatinine. In reporting their work on animals, Ashworth and his associates [15] pointed out repeatedly that the ratio of the basal metabolic rate to the preformed creatinine output decreases with increasing weight. In agreement with their findings, my values showed that although heat production and output of preformed creatinine followed a similar course, owing to the difference in the rate of increase, the ratio of the two decreased with augmentation of the size of the children and that both the ratio of the two and the output of preformed creatinine nitrogen were correlated more closely with body weight than with the other factors studied.

When my ratios of basal heat production to preformed creatinine nitrogen output are compared with the values reported by Talbot,[5] my figures are invariably higher. The averages for his 7 to 8, 9 to 10, 11 to 12, and 13 to 15 year old groups were 5.45, 4.29, 3.21, and 3.17, respectively, as compared with 6.55, 5.25, 4.24 and 3.85, the corresponding values for my children. Table 5 shows that although his children

16. Palmer and others.[1] Takahira.[2] Guhr.[3] Eimer.[4] Talbot.[5]

were on the average a year younger than mine, they were better developed. They weighed more and had higher creatinine coefficients. But their average basal heat production per kilogram of body weight was much lower than that of my children. Consequently, the ratio of basal metabolic rate to preformed creatinine nitrogen output was lower than that of my subjects.

In view of the fact that for this group of children the basal heat production and the preformed creatinine output did not run parallel at all ages and that not only were the ratios of the basal metabolic rates to the preformed creatinine nitrogen levels of the different children not constant but the values for my children were considerably different from those for the children of corresponding ages studied by Talbot, it is evident that more work along this line is necessary before the level of urinary creatinine can safely be employed as a standard for basal heat production.

TABLE 5.—*Comparison of Ratios Obtained in My Study with Ratios Reported by Talbot*

Author	Talbot		My Series	
Number of children	13		47	
	Range	Average	Range	Average
Age, years	7-14	10	7-15	11
Weight, Kg.	18.2-60.2	32	15.2-52.9	31
Creatinine nitrogen per Kg., mg.	5.8-10.4	8.3	6.7-9.3	8.1
Calories per Kg.	27-47	35	26-69	39
Calories per mg. creatinine nitrogen	3.02-6.19	4.39	3.00-7.66	4.83

SUMMARY

1. Under the age of 5 years the twenty-four hour values for basal heat production of 70 children increased much more rapidly than those for the preformed creatinine nitrogen output. Between the ages of 5 and 11 the increase for preformed creatinine nitrogen output exceeded that for basal metabolic rate. Thereafter the two curves ran nearly parallel until about the age of 14 years, when the rate of rise of the preformed creatinine nitrogen output again exceeded that of the basal metabolic rate.

2. Beginning at the age of approximately 6 months, the per kilogram values of the basal metabolism declined slowly and steadily throughout childhood, while those of the preformed creatinine level increased steadily until about the age of 10 years, when they began to approach constancy.

3. Basal metabolism expressed in terms of calories per milligram of preformed urinary creatinine nitrogen followed a course similar to that of calories per kilogram of body weight.

4. Values for total creatinine followed the same trend as those for preformed creatinine, except that they were less consistent.

5. With the exception of the values for basal metabolism expressed in terms of calories per milligram of preformed and total creatinine nitrogen output, the correlation coefficients of which were all negative, the coefficients of correlation of all factors studied were positive and unusually high. The preformed creatinine nitrogen output was most closely correlated with body weight and least with basal metabolism expressed as total calories per twenty-four hours, which was most closely correlated with height.

6. Except for the girls of the 13 year old group, for whom the preformed and the total creatinine values were higher and those for basal metabolism in terms of calories per milligram of preformed creatinine were lower, sex had no demonstrable influence on the total per twenty-four hour values. With a few exceptions, the per kilogram values of all factors tended to be lower for girls than the corresponding values for boys.

7. Owing to the facts that the basal metabolic rate and the preformed creatinine content did not run parallel at all ages for this group of children, that the ratio between the two was not constant and that the values in the present study varied considerably from those reported by Talbot, it is suggested that some other factor or factors aside from active protoplasmic tissues may be responsible for production of either basal heat or creatinine or of both and that more work is therefore necessary before preformed creatinine values can be safely employed as a standard for basal metabolism.

Drs. L. J. Roberts, of Chicago, and E. L. Sevringhaus, of Madison, Wis., gave suggestions and criticisms.

CIRCULATORY FUNCTION IN THE ANEMIAS OF CHILDREN

III. ALTERATIONS IN THE ELECTROCARDIOGRAM

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Pathologic conditions of the myocardium are frequently reflected by alterations in the form of the electrocardiogram. In view of this, it is remarkable that only a few descriptions of electrocardiographic abnormalities associated with anemia have appeared. This is especially noteworthy if anoxemia plays an essential role in both anemia and coronary occlusion, for the latter condition yields one of the most distinctive of all electrocardiographic tracings. Severe anemia, especially if it is chronic, is recognized as a cause of myocardial damage. Pathologically, such damage is manifested by dilatation, hypertrophy or degeneration, changes generally conceded to be the result of oxygen starvation. Clinical evidence of damage is provided by gradual enlargement of the heart, the development of murmurs and occasionally, especially in adults, the onset of heart failure, either congestive or anginal.[1] The fact that angina pectoris may be a complication of anemia [2] and may sometimes be relieved when the blood disorder is treated lends support to the widely accepted theory that oxygen depletion is an important factor in the mechanism which produces the symptoms of angina pectoris.[3] Coronary occlusion is in many ways closely related

* Dr. Parsons' work was done during the tenure of the Walter Meyers traveling studentship.

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1. Bartels, E. C.: Anemia as a Cause of Severe Congestive Heart Failure: Report of a Case, Ann. Int. Med. **11**:400, 1937.

2. (*a*) Herrick, J. B., and Nuzum, F. R.: Angina Pectoris: Clinical Experience with Two Hundred Cases, J. A. M. A. **70**:67 (Jan. 12) 1918. (*b*) Stalker, H.: Angina Pectoris and Pernicious Anemia: A Résumé of the Literature with a Case Report, Ann. Int. Med. **10**:1172, 1937.

3. Keefer, C. S., and Resnik, W. H.: Angina Pectoris: Syndrome Caused by Anoxemia of the Myocardium, Arch. Int. Med. **41**:769 (June) 1928.

to angina pectoris, and it is probable that oxygen lack is responsible, at least in part, for the features common to both diseases.

If deprivation of oxygen consequent on myocardial ischemia is a primary cause of the symptoms and electrocardiographic changes associated with occlusion of the coronary arteries, it is to be expected that a similar type of electrocardiogram will be seen in all conditions in which the amount of oxygen carried to the heart is reduced, i. e., angina of cardiosclerotic origin, anoxemia and anemia. Curves resembling those obtained in cases of coronary occlusion have, in fact, been seen during an attack of angina pectoris,[4] but the electrocardiogram rapidly reverts to normal as the pain subsides, so that during quiescent periods the tracing may be normal. In anginal subjects, however, measures known to be capable of producing a paroxysm of pain (exercise, induced anoxia or the injection of epinephrine, solution of posterior pituitary or insulin) will frequently bring out such typical alterations in the electrocardiogram.[5] This holds true even when the stimulus is not quite sufficient to produce anginal symptoms.[5e] Similar abnormalities are found when normal subjects are exposed to severe anoxemia,[5h] induced, for example, by carbon monoxide poisoning or by the breathing of mixtures of nitrogen and a low percentage of oxygen. They appear in normal persons also after a large dose of epinephrine;[5h] but apparently never as a result of exercise.[5a] On the other hand, it has rarely been pos-

4. (*a*) Bousfield, G.: Angina Pectoris: Changes in Electrocardiogram During Paroxysm, Lancet **2**:457, 1918. (*b*) Parkinson, J., and Bedford, D. E.: Electrocardiographic Changes During Brief Attacks of Angina Pectoris: Their Bearing on the Origin of Anginal Pain, ibid. **1**:15, 1931.

5. (*a*) Wood, F. C., and Wolferth, C. C.: Angina Pectoris: Clinical and Electrocardiographic Phenomena of Attack and Their Comparison with the Effects of Experimental Temporary Coronary Occlusion, Arch. Int. Med. **47**:339 (March) 1931. (*b*) Levine, S. A.; Ernstene, A. C., and Jacobson, B. M.: Use of Epinephrine as Diagnostic Test for Angina Pectoris, with Observations on Electrocardiographic Changes Following Injections of Epinephrine into Normal Subjects and into Patients with Angina Pectoris, ibid. **45**:191 (Feb.) 1930. (*c*) Milles, G., and Smith, P. W.: Effects of Epinephrine on the Heart, Am. Heart J. **14**:198, 1937. (*d*) Smith, K. S.: Nutrition of the Heart in Relation to Electrocardiogram and Anginal Pain, Lancet **1**:632, 1933. (*e*) Katz, L. N.; Hamburger, W. W., and Schutz, W. J.: Effect of Generalized Anoxemia on the Electrocardiogram of Normal Subjects: Its Bearing on the Mechanism of Attacks of Angina Pectoris, Am. Heart J. **9**:771, 1934. (*f*) Rothschild, M. A., and Kissin, M.: Production of Anginal Syndrome by Induced General Anoxemia, ibid. **8**:729, 1933. (*g*) Katz, L. N., and Landt, H.: Effect of Standardized Exercise on Four-Lead Electrocardiogram: Its Value in the Study of Coronary Disease, Am. J. M. Sc. **189**:346, 1935. (*h*) Rothschild, M. A., and Kissin, M.: Induced General Anoxemia Causing S-T Deviation in the Electrocardiogram, Am. Heart J. **8**:745, 1933. (*i*) Katz, L. N.; Hamburger, W. W., and Lev, M.: Diagnostic Value of Epinephrine in Angina Pectoris, ibid. **7**:371, 1932.

sible to demonstrate such electrocardiographic variations in cases of anemia in man, despite the fact that they have been successfully duplicated in animals during the process of bleeding.[6]

The changes in the electrocardiogram which have been described as occurring in the presence of the various conditions consist of flattening or inversion of the T waves in one or more leads and, frequently, deviation of the ST segment from the isoelectric level; they differ from the curves observed in cases of coronary occlusion in that the deviation of the ST segment is in the same instead of the opposite direction in leads I and III. Prolongation of auriculoventricular conduction time has been described also.[7] In contrast, the effect of exercise on normal persons is to increase the amplitude of the T waves (except sometimes in lead I), to shorten the PR interval and to leave the ST segment unaltered.

It has been remarked that anginal patients may not present a characteristic electrocardiogram unless cardiac work is deliberately increased, and it is reasonable to suppose that the same condition may apply to patients with anemia. Since anoxia and the injection of epinephrine may lead to alterations in the electrocardiogram even with normal subjects and since insulin introduces factors other than oxygen deficiency, exercise seems to be the method of choice and the most natural way of imposing strain on the heart and augmenting its need for oxygen. Anemic blood may be unable to carry sufficient oxygen to meet the greater demand of the myocardium, so that a state of relative anoxemia will develop. Pickering and Wayne,[8] in a study of the effect of exercise on the electrocardiograms of anemic subjects, were unable to obtain any positive results. Their failure is not necessarily of significance, as even the severe myocardial anoxemia which follows temporary occlusion of the coronary vessels does not invariably affect the electrocardiogram. Thus, Wood and Wolferth,[5a] working with dogs, remarked:

> Sometimes the experimental occlusion of a large coronary artery, with consequent production of a definite change in the appearance and action of the heart, caused no change in the electrocardiogram.

Wolferth and Wood[9] also pointed out the importance of the chest lead in the recognition of otherwise unidentifiable coronary disease; the

6. Radnai, P.: Ueber das elektrokardiographische Bild der durch akute Anämie verursachten Herzmuskelanoxämie, Ztschr. f. klin. Med. **128**:401, 1935.

7. (*a*) Lewis, T., and Mathison, G. C.: Auriculo-Ventricular Heart-Block as a Result of Asphyxia, Heart **2**:47, 1910. (*b*) Mathison, G. C.: The Cause of the Heart-Block Occurring During Asphyxia, ibid. **2**:54, 1910.

8. Pickering, G. W., and Wayne, E. J.: Observations on Angina Pectoris and Intermittent Claudication in Anemia, Clin. Sc. **1**:305, 1934.

9. Wolferth, C. C., and Wood, F. C.: Electrocardiographic Diagnosis of Coronary Occlusion by the Use of Chest Leads, Am. J. M. Sc. **183**:30, 1932.

use of this lead seemed of potential value in the present investigation. Studies of the chest lead with children have shown it to be of variable pattern even at different times in the same patient.[10] The T waves in the fourth lead are especially liable to change, and both upright and inverted T waves have been seen in the electrocardiograms of normal children. The ST segment is also subject to considerable variation and may show a deviation of as much as 2 mm. from the isoelectric line. It should be emphasized that this deviation is usually to the positive side of the isoelectric line.[10a]

MATERIAL AND METHOD

Five children[11] suffering from various forms of anemia (3 with erythroblastic anemia, 1 with aplastic anemia and 1 with anemia secondary to acute hemorrhage) and a control group of 10 normal children were selected for study. Electrocardiograms were obtained during rest. The children were then taken down in an elevator and required to return upstairs to the examining room, walking at a pace set by the examiner. The number of stairs climbed varied with the size and capability of the child, but the average height was 30 feet (three flights). The pace likewise varied, but the time taken was usually about fifty seconds. Electrocardiograms were made immediately. The anemic children were reexamined in the same manner after the anemia had been relieved by appropriate treatment.

Electrocardiograms were taken in the usual manner with the chest lead added to the three standard leads in every case. The point of contact chosen for the precordial electrode lay 2 inches (5 cm.) to the left of the midsternal line, in the fourth intercostal space. This site was selected because it has been demonstrated that with an enlarged heart, when the chest lead is taken from the cardiac apex, and therefore from a point on the lateral aspect of the thorax in the anterior or midaxillary line, the curve obtained resembles that of the third lead.[12] Moreover, as a result of exercise or treatment, the apical impulse might be expected to alter its position, thereby making it difficult to obtain comparable readings. In taking the chest lead we used the method which promises to be universally adopted:[13]

10. (*a*) Robinow, M.; Katz, L. N., and Bohning, A.: Appearance of T-Wave in Lead IV in Normal Children and in Children with Rheumatic Heart Disease, with Some Observations Concerning the Cause of T-Waves Obtained, Am. Heart J. **12**:88, 1936. (*b*) Rosenblum, H., and Sampson, J. J.: Study of Lead IV of the Electrocardiogram in Children with Especial Reference to Direction of Excursion of T-Wave, ibid. **11**:49, 1936. (*c*) Hafkesbring, E. M.; Drawe, C. E., and Ashman, R.: Children's Electrocardiograms: Measurements for One Hundred Normal Children, Am. J. Dis. Child. **53**:1457 (June) 1937. (*d*) Master, A. M.; Dack, S., and Jaffe, H. L.: Precordial Lead of the Electrocardiogram of Normal Children, ibid. **53**:1000 (April) 1937.

11. Parsons, C. G., and Wright, F. H.: Studies of the Circulatory Function in the Anemias of Children: I. The Effect of Anemia on Exercise Tolerance and Vital Capacity, Am. J. Dis. Child. **57**:15 (Jan.) 1939.

12. Roth, I. R.: Chest Lead Tracings in Arterial Hypertension with Cardiac Enlargement, Am. Heart J. **14**:155, 1937.

13. Standardization of Precordial Leads, special article, Am. Heart J. **15**:235, 1938.

moving the left leg electrode to the precordium and attaching the right arm lead to the left leg. In the normal adult this arrangement insures that the P and T waves are upright and that the tracing is thus brought into line with those of the other three leads.

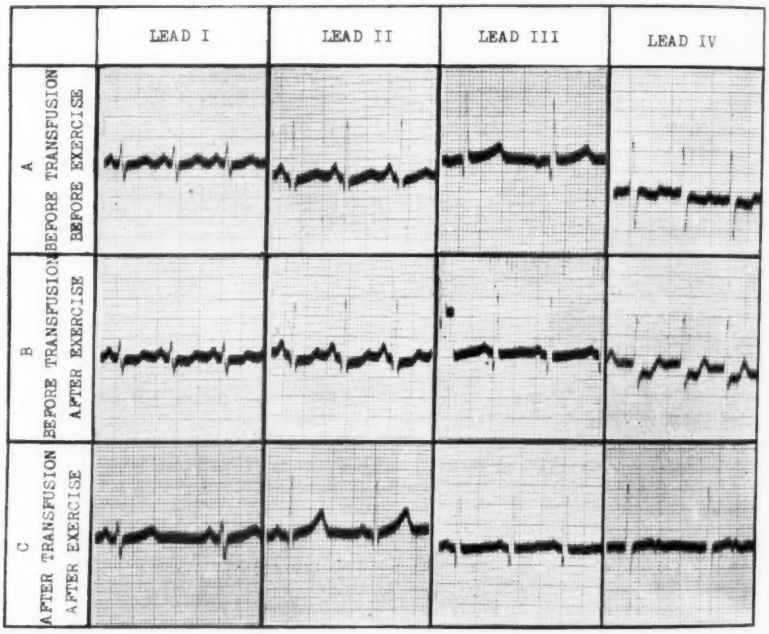
RESULTS

The electrocardiograms obtained after exercise for the normal subjects did not differ from what was expected in view of previous studies.[5a] The cardiac rate was accelerated; the PR interval and the duration of the ventricular complex were either unchanged or somewhat shorter. The P and QRS complexes were frequently, and the T waves almost invariably, greater in amplitude. In 2 cases the T waves were diphasic while the child was at rest and upright after exercise. The T waves were never flattened or depressed by exercise, even after the subject had climbed six flights of stairs as rapidly as possible. The pattern of the fourth lead, although it showed variations on different occasions in the same subject, was on the whole remarkably constant. With 3 subjects at rest, the ST segment in this lead was raised slightly above the isoelectric level, but never by more than 1 mm. In 2 of these 3 children the segment returned to the isoelectric line when exercise was taken, but in the third its position was not altered after exercise. In the other leads no deviation of the segment was noted, and in no instance was it depressed as a result of muscular work.

The electrocardiograms of the children with aplastic anemia (case 1) and acute secondary anemia (case 5) were essentially the same as those of the normal children. On the other hand, all 3 patients with erythroblastic anemia showed an abnormal response to exercise. In 2 of these (cases 3 and 4) the abnormality was not striking; the T waves, instead of increasing in size, became flatter after exertion. This change was present in at least two of the three standard leads and was considerably less conspicuous after treatment of the anemia. One of these 2 patients also showed a reduction in the size of the QRS complex after exercise, but treatment did not alter this finding. The auriculoventricular conduction time was not abnormally prolonged in the case of any of the anemic children, although as a rule it became slightly shorter after treatment. Deviation of the electrical axis was not seen.

The electrocardiograms for the third child with erythroblastic anemia (case 2) were more significant and are reproduced in the accompanying illustration. The child was admitted to the hospital with signs of congestive heart failure: She was dyspneic; the superficial veins were engorged, and there was mild edema of the ankles. The heart sounds were of poor quality, and gallop rhythm was audible at the apex, in addition to a systolic murmur which could be heard all over the precordium. All these signs except the systolic murmur disappeared with no treatment other than rest in bed, and not until their disappearance

was the first electrocardiogram taken. An essentially normal tracing was obtained with the child at rest. The rhythm was of sinal origin and was regular; the PR interval was not prolonged, and the complexes in all four leads were normal except for a deep Q_3 and an inverted P_3 complex. This inversion of P waves is difficult to explain, but has been previously described in cases of anemia.[14] Exercise was limited to the slow ascent of a single flight of stairs, which took nearly forty seconds. The electrocardiogram taken immediately afterward was remarkable chiefly for the depression of the ST segment below the isoelectric line in leads I, II and IV. This was least apparent in the



Electrocardiograms of the patient in case 2 before and after treatment, showing the effect of exercise during the anemic phase and after transfusion. Standardization is not absolutely accurate in lead IV (*B*), but after correction the deviation of the ST segment is still well outside normal limits.

first and most evident in the fourth lead. The T waves in lead III, which had been prominent before exercise, were flattened to the isoelectric line, while the P wave, which had been inverted in this lead, became upright. The curve was, indeed, of the type associated with severe anoxemia. A series of small blood transfusions was then given,

14. Porter, W. B.: Heart Changes and Physiological Adjustment in Hookworm Anemia, Am. Heart J. **13**:550, 1937.

which increased the erythrocyte count from 1,240,000 to 2,400,000 per cubic millimeter and the hemoglobin concentration from 2.4 to 7.7 Gm. per hundred cubic centimeters. An electrocardiogram taken after this procedure with the child at rest was similar to the record before transfusion except that the P_3 wave had become upright, the Q_3 wave shallower and the T waves greater in amplitude. Sinal arrhythmia was more conspicuous, and the cardiac rate was slower. There was, however, a great contrast between the records taken after exercise, for even when four flights were climbed in a little over sixty seconds the increase in the cardiac rate was less pronounced and sinal arrhythmia persisted. Except for a tendency for the T waves to decrease in size and for the Q_3 wave to become deeper, the record was not abnormal. The depression of the ST segment, which had been so striking in the corresponding record before treatment, was absent and could not be reproduced. In fact, much that had been considered characteristic evidence of anoxemia had disappeared (fig.).

COMMENT

Coombs [15] concluded that in cases of pernicious anemia a typical electrocardiographic abnormality could be detected. His patients, like nearly all those in whose cases similar unusual features have been described, were adults suffering from angina pectoris, and the possible coexistence of coronary vascular disease could not be entirely ignored. A case was reported by Elliott [16] in which, despite the presence of anginal symptoms, autopsy revealed no evidence of coronary sclerosis. Elliott ascribed both the symptoms and the electrocardiographic abnormalities, which included depression of the ST segment, to the presence of anemia.

Porter [14] found that the electrocardiogram was affected in almost 40 per cent of a series of patients suffering from anemia due to hookworm. Most common were alterations in the electrical axis of the ventricles, left preponderance being especially frequent. Changes in the contour of the T waves and prolongation of the PR interval were also seen. In a case in which he observed inverted PR and T waves in lead III he was unable to rule out a diagnosis of congenital morbus cordis. The only other patient whose electrocardiogram showed inversion of the T waves had also transient prolongation of the PR interval, but Porter concluded that this increase in conduction time might be due to a bout of fever, of unknown origin. Four children were included

15. Coombs, C. F.: Cardiac Symptoms of Pernicious Anemia with Particular Reference to Cardiac Pain, Brit. M. J. **2**:185, 1926.

16. Elliott, A. H.: Anemia as a Cause of Angina Pectoris in the Presence of Healthy Coronary Arteries and Aorta: Report of a Case, Am. J. M. Sc. **187**: 185, 1934.

in his group of patients, and 2 of these had normal electrocardiograms. Of the other 2, 1 presented flattened P waves in the second and third leads with a large Q wave in lead III; the other was the patient mentioned, in whose case congenital cardiac disease could not be excluded. There was little alteration in the curves after the anemia had been treated.

Prolongation of the PR interval with return to normal after improvement of the blood picture was noted by Pickering and Wayne [8] in 2 of a series of 10 patients. One patient had anginal symptoms and a left axis deviation, both of which persisted after treatment and recovery from the anemia. The remaining patients had normal electrocardiograms, and in 3 of them exercise produced no change.

Bloch [17] made an electrocardiographic study of the relation between angina pectoris and anemia in 37 adults with anemia. He classified the positive findings under three headings: (1) low voltage, (2) depression of the ST segment in two or more leads, and (3) flattening of the T waves. Deformities of the T waves were present in 51 per cent of his cases. Depression of the ST segment, so common in coronary disease, was more infrequent, occurring in only 5 cases. This proportion is probably unusually high. One of these 5 patients suffered from angina pectoris, and since no pathologic examination was made in any case the existence of coronary vascular disease could not be specifically denied.

Except for the 2 cases cited by Porter, we have been unable to find any reports of cases in children in which alteration in the form of the electrocardiogram was a direct result of anemia. Unfortunately, for reasons which he himself had given, neither of Porter's cases was particularly convincing. Even adults known to be free from coronary sclerosis seldom have electrocardiograms showing the changes typical of anoxemia. Reid [18] examined 20 patients with severe anemia, with specific attention to such changes; Smith [5d] examined 15 patients with the same point in mind; Willius and Giffin [19] observed 12 adults with anemia, and Hochrein and Matthes [20] studied the electrocardiograms of 32 such patients. None of these investigators was able to report any significant finding. The subject had been summed up by Stalker,[2b] who,

17. Bloch, C.: Angina pectoris und Anämie, Wien. Arch. f. inn. Med. **26**: 143, 1934.

18. Reid, W. D.: Heart in Pernicious Anemia, J. A. M. A. **80**:534 (Feb. 24) 1923.

19. Willius, F. A., and Giffin, H. Z.: Anginal Syndrome in Pernicious Anemia, Am. J. M. Sc. **174**:30, 1927.

20. Hochrein, M., and Matthes, K.: Anämie und Angina pectoris, Deutsches Arch. f. klin. Med. **177**:1, 1934.

after reviewing the literature on more than 100 cases of angina pectoris due to anemia, stated:

> In general the consensus of opinion has been that there were no diagnostic abnormalities in the electrocardiograms, and what changes were noted could be traced to coincident cardiosclerosis.

While we agree with Stalker that anemia produces no change in the electrocardiogram by which its presence may be recognized, we believe the present investigation has shown that anemia may lead to deformities in the electrocardiogram even when disease of the coronary vessels is absent. Although pathologic material proving the absence of coronary disease is lacking in the cases which we observed, the occurrence of coronary sclerosis in childhood is so rare that its presence in 3 of 5 cases selected at random from a pediatric clinic for anemic patients would be almost outside the realm of possibility. The few (9) autopsy reports to which we have access do not record the observation of coronary sclerosis in children who died of erythroblastic anemia. The point deserves further examination. The occurrence of electrocardiographic changes only in the patients with erythroblastic anemia is probably coincidental. We believe that similar abnormalities might be demonstrated in a large percentage of children suffering from any form of severe chronic anemia.

The evidence which we have collected is suggestive that the changes seen in the electrocardiogram were due to oxygen starvation: 1. In none of the cases in which there were positive findings was any change in the electrocardiogram demonstrated with the patient at rest, but when the demand of the heart for oxygen was increased through the performance of work, a state of relative anoxemia probably being induced, the electrocardiographic findings became positive. 2. These findings correspond to a greater or less degree with those which are known to be produced by anoxemia and are precisely the reverse of those seen after exertion in the normal subject. 3. After the oxygen-carrying capacity of the blood had been improved by treatment the effect of exercise on the electrocardiogram was more nearly normal, despite the fact that the blood counts never attained optimal levels.

The importance of such observations might easily be exaggerated; our excuse for recording them lies in the absence (to our knowledge) of previous definite evidence that anemia alone may alter the form of the human electrocardiogram. Depression of the ST segment is seldom observed unless anoxemia is relatively severe, and, except for the case described by Elliott, no instance of its occurrence in an anemic patient with healthy coronary vessels has been reported.

An interesting point which became apparent in the investigation of these children was the normal response to exercise tolerance as based

on changes in the pulse rate and the rapidity of its fall to normal [11] even when the electrocardiographic characteristics of anoxemia were most prominent. This throws doubt on one of the common tests of cardiac function when used in the presence of anemia, since in this instance it is certain that myocardial impairment was present and responded to treatment.

The improvement of the electrocardiographic tracing after transfusion suggests that the myocardial damage due to anemia will respond to treatment and is not necessarily permanent. Recent work has shown that the duration of the period during which the myocardium is exposed to ischemia is all important in determining whether the cardiac damage is permanent or transitory.[21] If the coronary arteries of the cat are clamped for five to ten minutes the electrocardiogram and myocardial function are adversely, but temporarily, affected, but in general recover eventually. If the occlusion is maintained for fifteen minutes the cardiac changes are permanent. This emphasizes the need for keeping the oxygen-carrying powers of the blood at a high level in patients suffering from a severe degree of anemia.

SUMMARY

Changes resembling those observed in experimental and clinical states of myocardial anoxemia were found in the electrocardiograms of children suffering from chronic anemia. The use of exercise in making them manifest is discussed.

The electrocardiograms were obtained through the cooperation of the department of cardiology of the Presbyterian Hospital.

21. Blumgart, H. L.; Hoff, H.; Landowne, M., and Schlesinger, M. J.: Experimental Studies on the Effect of Temporary Occlusion of Coronary Arteries in Producing Persistent Electrocardiographic Changes, Am. J. M. Sc. **194**:403, 1937.

EMPHYSEMA OF A PORTION OF THE LUNG IN THE EARLY MONTHS OF LIFE

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Emphysema of a portion of the pulmonary tree has been noted and its pathogenesis discussed by many observers. Schenk [1] ascribed to Bartholinus the first description of cystic lung published in 1687, but he did not state whether the condition was emphysematous. Kountz and Alexander [2] credited Laënnec with having originated, in 1819, the idea of partial bronchial obstruction as a factor in the production of emphysema. Localized emphysema is often associated with cystic disease of the lung, and the two conditions are frequently discussed together. The first case discussed by Meyer,[3] in 1856, was an instance of cystic disease associated with emphysema of the upper lobe of the left lung. Many others have reported the two conditions as occurring simultaneously.

The course of events leading to emphysema depends on an increase in the amount of residual air in the lung. At birth, before the baby has taken a breath, intrapleural and intrabronchial pressure are neutral or atmospheric, so far as is known, although there has been a recent revival of interest in the idea that fetal respiratory movements suggest a flow of amniotic fluid through the respiratory tree before birth.[4] From this time, the elasticity of the lung maintains a negative intrapleural pressure except in forced expiration. There is evidence to indicate that in the asthmatic lung during an attack the intrapleural pressure is more negative than normal until the elasticity of the lung

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1. Schenk, S. G.: Diagnosis of Congenital Cystic Disease of the Lung, Arch. Int. Med. **60**:1-21 (July) 1937.

2. Kountz, W. B., and Alexander, H. L.: Emphysema, Medicine **13**:251-356 (Sept.) 1934.

3. Meyer, H.: Ueber angeborene blasige Missbildung der Lungen, nebst einigen Bemerkungen über Cyanose aus Lungenleiden, Virchows Arch. f. path. Anat. **16**: 78-95 (Jan.-Feb.) 1859.

4. Bonar, B. E.; Blumenfeld, L. M., and Fenning, C.: Studies of Fetal Respiratory Movements: I. Historical and Present Day Observations, Am. J. Dis. Child. **55**:1-11 (Jan.) 1938.

is lost,[5] when it may become more positive. One must assume that intrabronchial and intra-alveolar pressures are greater than intrapleural pressure in the normal lung.

Hoover ([5a]) demonstrated that bronchial resistance in the dog increases the residual air only when the resistance to expiration is greater than the resistance to inspiration, and then only when hyperpnea attains such a degree that the respiratory need does not allow adequate time for the volume of the expired air to equal that of the inspired air. He also found that compression of the lungs in expiration does not produce a vicious cycle of increasing resistance to expiration. Bronchoscopists [6] have reported that in the normal bronchial tree there are elongation and expansion of the bronchi with inspiration and shortening and constriction with expiration. This has also been demonstrated by means of a rapidly taken succession of roentgenograms of the lung filled with iodized poppyseed oil, which give the effect of a moving picture.[7] Hoover [5a] observed that partial expiratory obstruction of one bronchus produced emphysema of the lobe supplied by that bronchus. This implies that there must be a space for the expanded portion of the lung to occupy, i. e., the more easily compressed remaining lobes. In checking this by animal experimentation, he found that with a flap valve obstructing expiration but allowing free inspiration in one lung, that lung became emphysematous at the expense of the available space, the other lung and the space at the lower portion of the pulmonary field by depressing the diaphragm. Van Allen [8] went one step further and demonstrated that expiratory, but not inspiratory, obstruction of an entire lobe led to emphysema of that lobe but that if smaller units were so treated they did not become emphysematous, owing to collateral circulation of air. Bronchoscopists have reported similar experiences in the presence of check valve mechanisms.[6] Kountz and Alexander [2] stated the belief that with generalized emphysema there are spasm and actual hypertrophy of the muscle fibers of the 3 to 8 mm. bronchioles and that after inspiratory distention of the

5. (*a*) Hoover, C. F.: Tracheal and Bronchial Stenosis as a Cause for Emphysema, Arch. Int. Med. **29**:143-167 (Feb.) 1922. (*b*) Christie, R. V.: Elastic Properties of Emphysematous Lung and Their Clinical Significance, J. Clin. Investigation **13**:295-321 (March) 1934. (*c*) Prinzmetal, M.: Relation of Inspiratory Distention of the Lungs to Emphysema, J. Allergy **5**:493-504 (July) 1934.

6. Jackson, C.: The Mechanism of Physical Signs with Especial Reference to Foreign Bodies in the Bronchi, Am. J. M. Sc. **165**:313-320 (March) 1923.

7. Hudson, W. A., and Jarre, H. A.: Functional Studies of the Tracheobronchial Tree with the Aid of the Cin-ex Camera, Brit. J. Radiol. **2**:523-533 (Nov.) 1929.

8. Van Allen, C. M.: Obstructive Pulmonary Emphysema and Collateral Respiration, Surg., Gynec. & Obst. **55**:303-307 (Sept.) 1932.

smaller lobules these air passages may constrict and maintain a state of increase in residual air. This is compatible with the findings of Van Allen only if all adjoining lobules are affected at the same time, as is probably true.

A few cases of localized emphysema not associated with cystic malformations of the bronchial tree or not consisting of subpleural emphysematous blebs have been reported. There have been many more in which cystic disease has been complicated by emphysema.

Wethered [9] in 1897 reported a case of hypertrophy of the upper lobe of the right lung in a patient 51 years old. The bronchus leading to this lobe was large, and no obstruction was noted. The middle and the lower lobe of the right lung were small, and Wethered diagnosed the condition as compensatory emphysema following pneumonia, which the patient had had in childhood. Hoover [5a] reported a case in an adult who had an aneurysm of the arch of the aorta, the emphysema being present only when the patient was lying down. Peeler and Phillips [10] cited a case of a 2 month old infant in whom the bronchus leading to the affected upper lobe of the left lung was much smaller than normal. There were no histologic observations. Nelson [11] described a somewhat similar case, in which the bronchus of the involved upper lobe of the left lung was smaller and contained fewer cartilaginous rings than usual. The bronchi and alveolar spaces were dilated, and there was a small accessory lobe of the lung tissue on the lower portion of the upper lobe of the left lung. Morelli [12] discussed the possibility that an aberrant pulmonary artery can produce a similar picture.

REPORT OF A CASE

T. W. M. was born on Jan. 26, 1937, at full term, by vertex presentation and spontaneous delivery. The weight was 3,864 Gm. The mother was 21 years old and had been married ten months. During the sixth month of her pregnancy a rash appeared which was diagnosed as secondary syphilis, and therapy was begun in the outpatient clinic of the University of Oregon Medical School. Treatment was regular and adequate until the termination of pregnancy. The father, aged 25 years, also had active syphilis; this was discovered at the same time, and treatment was begun. The child nursed well and regained his birth weight on the eighth day of life. He was dismissed on the thirteenth day, in good condition. The Wassermann and Kahn reactions of the cord blood were strongly positive, as

9. Wethered, F. J.: A Case of Hypertrophy of the Lung, Tr. Path. Soc. London **48**:34-37, 1897.

10. Peeler, C. N., and Phillips, C. C.: Some Observations on Endoscopy, South. Med. & Surg. **84**:299-303 (June) 1922.

11. Nelson, R. L.: Congenital Cystic Disease of the Lung, J. Pediat. **1**:233-238 (Aug.) 1932.

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were those of the mother's serum. At the age of 3 weeks the child's Wassermann reaction was anticomplementary, and at the age of 1 month the reactions to both tests were negative and remained so. Roentgenograms of the long bones taken on the third day of life showed no destructive process or periosteal reaction. In these films it was noted that there was hyperaeration of the upper portion of the left lung. There were no respiratory symptoms at the age of 3 weeks. When the baby was 1 month of age, the mother noted that he had attacks of difficult respiration in which each breath was accompanied by a grunt and that with the attacks the hands and feet became blue. At this time it was noted that there was a grunt at the beginning of expiration and that breathing was abdominal. The mediastinum was displaced to the right; the apex beat was on the right side of the sternum; the left side of the chest was tympanitic, and the breath sounds were absent on that side except at the apex. The baby was admitted to the hospital for observation. The urine was normal. The hemoglobin content was 9.17 Gm. per hundred cubic centimeters of blood; there were 3,530,000 red cells per cubic millimeter and 6,500 leukocytes, of which polymorphonuclears comprised 39 per cent, eosinophils 5 per cent, lymphocytes 47 per cent and degenerated cells 2 per cent. The sedimentation rate was 2 mm. at fifteen minutes and 13 mm. at forty-five minutes. The reaction to 0.1 mg. of tuberculin was negative.

The patient remained in the hospital for one month. The weight fluctuated between 4,126 and 4,290 Gm. The appetite was poor, and the child regurgitated frequently. Diarrhea developed, with blood and mucus in the stool. Culture revealed no organisms which did not ferment lactose. The diarrhea improved, and after a month's stay in the hospital the patient was sent home to convalesce, as surgical intervention was thought inadvisable at that time.

Five days later he was readmitted because of recurrence of the diarrhea and failure to take food. In addition to the findings previously noted, subcostal retraction was present. After the diarrhea had subsided, the patient was seen by Dr. Ralph Matson, who advised aspiration of the involved area and insertion of a tube with a water valve which would permit only exit of the trapped air. This was performed on April 13. Aspiration gave only temporary relief. Injected iodized poppyseed oil was seen to lodge in what was assumed to be dilated alveoli of the lung. Intrapleural pressure was measured and found to be strongly positive in all phases of respiration. The degree of pressure could not be accurately measured because of the child's struggles. A tube inserted into the lung substance failed to give appreciable relief, although air left the tube with each expiration.

Serial roentgenograms were taken (fig. 1).

The baby contracted bronchopneumonia of the right lung with a small pleural effusion and died on May 29.

Postmortem Examination.—This was performed by Dr. Warren Hunter and the staff of the department of pathology.

Gross Description: The external appearance was not remarkable except for a trocar wound in the fourth interspace of the left side of the chest in the anterior axillary line. The heart was displaced to the right, owing to obvious emphysema of the upper lobe of the left lung, which had compressed the lower lobe and the entire right lung. The right chambers of the heart were dilated and hypertrophied. The right lung was the seat of slight purulent pleuritis and had increased consistency. There was an accessory lower lobe on the left. The thymic body was displaced to the right.

The other major cavities of the body were normal, as were the other organs.

Three specimens of the thoracic organs were dissected.

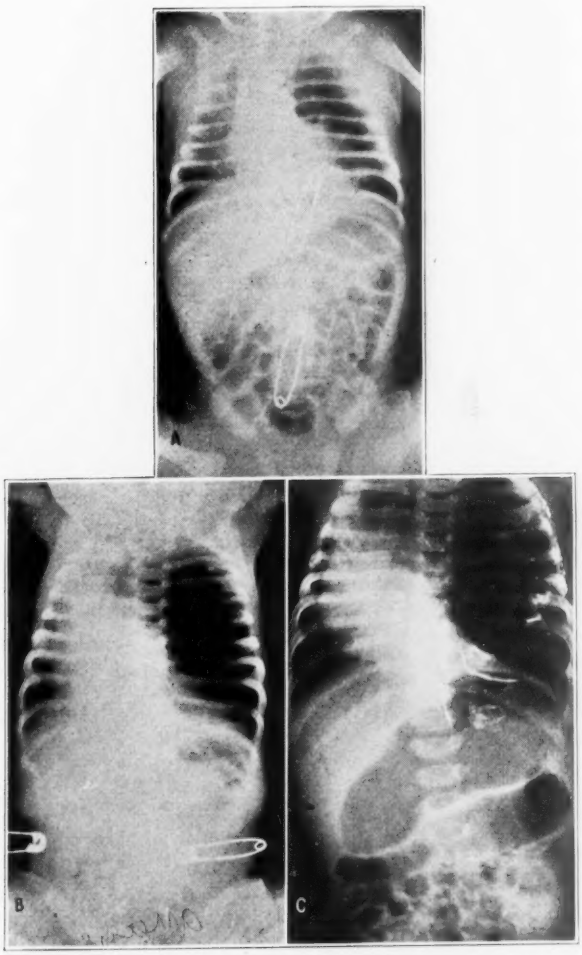

Fig. 1.—*A*, roentgenogram taken on the third day of life, three weeks prior to the onset of symptoms, in a search for evidence of syphilis of the bones. There is some hyperaeration of the upper lobe of the left lung with shift of the mediastinum to the opposite side. *B*, was taken at the age of 1 month. At this time there were symptoms of dyspnea and cyanosis on exertion. Depression of the diaphragm and marked shift of the mediastinum were present, as well as increase in the hyperaeration. Fluoroscopic study showed little motion and no paradoxic motion of the left leaf of the diaphragm. *C* was taken at the age of 4 months, shortly before death. Radio-opaque oil injected into the lung substance was diffusely distributed, as is seen in the upper portion of the upper lobe of the left lung. The apparent pocketing of the oil at the levels of the tenth and twelfth ribs is due to collections in the costophrenic sinus. There has been marked increase in the deformities previously noted.

Fig. 2.—Photograph showing dilatation of the upper lobe of the left lung after removal of the chest plate and inflation of the lung with a fixing agent.

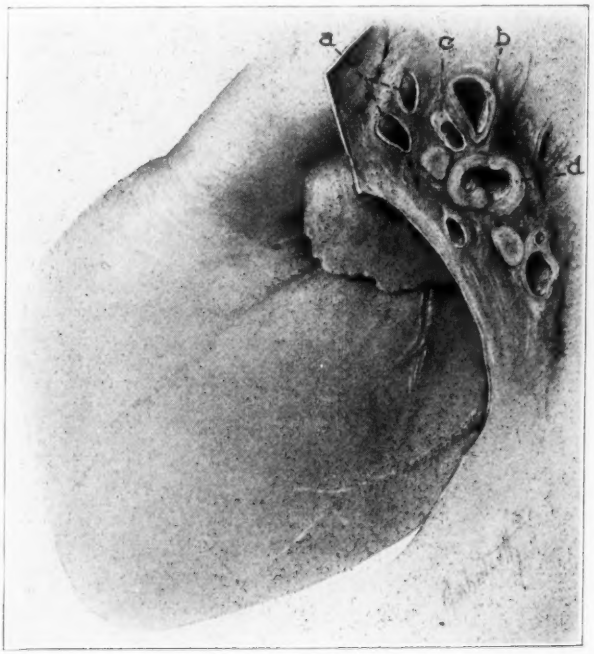

Fig. 3.—Drawing of the left side of the heart and the hilar structures. Branches of the pulmonary vein (*a*) and of the pulmonary artery (*b*) lie above the collapsed bronchus to the upper lobe (*c*). The normal bronchus to the lower lobe is seen below (*d*).

One consisted of the heart and mediastinal structures, including portions of the esophagus, trachea, pulmonary arteries and aorta. The heart had a maximum transverse diameter of 5 cm. The right ventricle of the heart occupied the larger portion of the anterior surface. Its maximum transverse diameter was 4.2 cm. The pulmonary conus was prominent. The right auricular appendage was distended with blood. The pericardial surface was smooth. The right ventricle was definitely dilated. The trabeculae carneae were nevertheless prominent, and the wall of the right ventricle was increased in thickness. Its average thickness at the base was 5 mm., in the central portion 6 mm. and at the apex 6 mm. The right auricle and the right auricular appendage were dilated, but there was no definitely recognizable increase in the thickness of the walls, although the trabecular markings were prominent. The left ventricle was thick walled and of small capacity. Its average thickness at the base was 1.1 cm., at the center 1.2 cm. and at the apex 1 cm. No unusual changes were seen in the various cardiac valves. The foramen ovale was almost completely closed, although a small probe could be passed through it. The relation of the great vessels of the heart were normal.

The trachea was smooth-walled, and its mucosa was pale. This was true of the main bronchi. The main bronchus to the upper lobe of the left lung arose about 2 cm. below the tracheal bifurcation. Its orifice was slitlike, measuring 2.5 mm. in length and less than 1 mm. in width. Immediately beyond its beginning, the bronchus increased slightly in diameter, so that at the point at which it was sectioned (fig. 4) it had a maximum diameter of 3.5 mm. and a minimum diameter of 1.5 mm. The main bronchus to the lower lobe of the left lung, on the contrary, was rounded and had a maximum diameter of 4.5 mm. The wall of the lower part of the main bronchus was much thicker than that of the upper part. It measured up to 1.5 mm. in thickness. The upper branch, however, never attained a thickness of as much as 1 mm. Its posterosuperior portion was extremely thin. Here the wall of the bronchus obviously contained no cartilaginous tissue. The anteroinferior portion of the bronchus was more rigid, and the appearance of this area approached that of a normal structure. The portion of the main bronchus of the upper lobe of the left lung shown in figure 4 lay immediately below the first bifurcation of the pulmonary artery.

The aorta and esophagus were unaltered. The right main bronchus arose normally and had a normal-appearing thick, rigid wall.

The upper lobe of the left lung, as viewed anteriorly, occupied 8 cm. of the entire 9 cm. of the perpendicular length of the lung. Posteriorly the lobe attained a maximum length of 7 cm.; the upper lobe comprised about four fifths of the entire lung. The surface of this lobe was covered by dense bands and tags of fibrous connective tissue. There were a few similar adhesions over the lower lobe, but for the most part this lobe was smooth. The upper lobe was spongy in consistency, while the lower lobe was firm. The cut surfaces showed a diffuse but striking increase in the size of the air sacs, which were readily visible. They appeared to have four or five times the diameter of those of the lower lobe. The right lung was generally firm in consistency, and lacking in crepitation. After fixation in a solution of formaldehyde the left lung weighed 130 Gm., and the right, 120 Gm.

Microscopic Description: Microsections cut to include the left main bronchus, with the portion which appeared grossly to be narrowed, the surrounding connective tissue, two lymph nodes and the main pulmonary artery revealed no abnormalities of development of the bronchus. Here there was a great loss of epithelium through desquamation, with the basement membrane often left exposed. In the submucosa were patches of polymorphonuclear neutrophils with engorged blood

vessels and a few lymphocytes and monocytes. The stenosed branch of the bronchus abutted directly against the parent bronchus but was separated from it by perichondrium, connective tissue and a little fat and was possessed of entirely separated cartilages. The significant feature about this bronchus, the one that probably explains why it collapsed, was the lack of a complete ring of cartilage, there being a deficiency of cartilage along the thin side. In other words, this bronchus resembled the trachea in structure in that it possessed a bare area. Its wall was otherwise complete, although the muscularis mucosae along the area of deficiency was thinner and much more frayed than it should have been, and there appeared to be also some diminution in the number of mucous glands. At the thinnest point, then, the

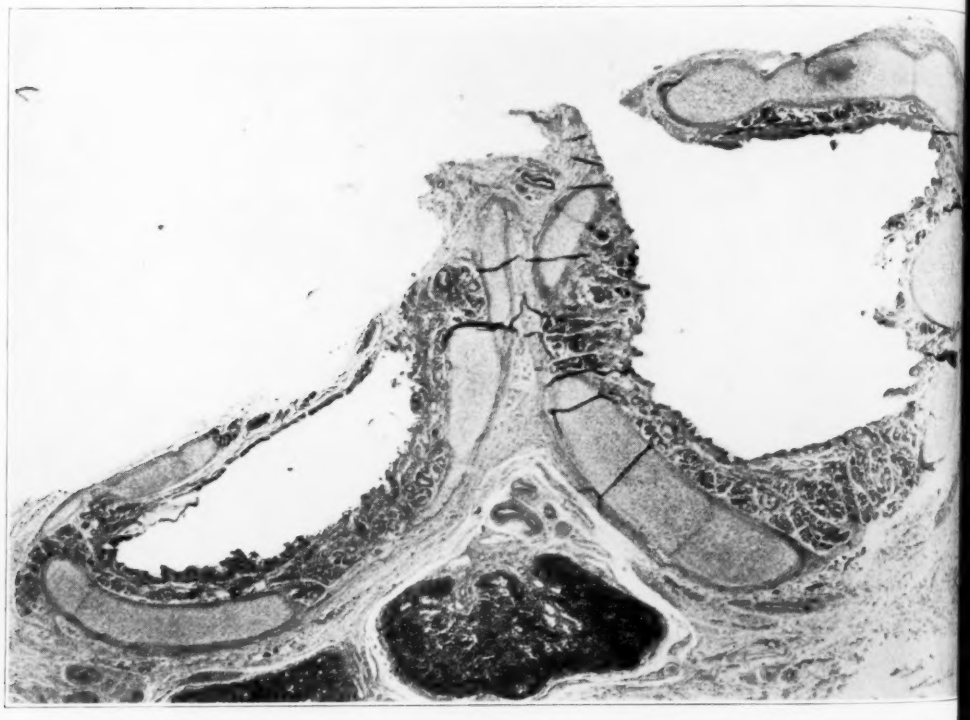

Fig. 4.—Low power photomicrograph of the main bronchus to the lower lobe of the left lung (larger) and of the bronchus to the upper lobe of the left lung (smaller), together with peribronchial connective tissue and lymph nodes. The smaller bronchus is deficient in cartilage along the flattened upper border and thus is analogous to the trachea in structure. The opening in the lower bronchus is a scissors' cut. In both bronchi much of the mucosa had desquamated after death. The several black lines over the cartilage represent folds in the section.

wall consisted of mucosa, submucosa and connective tissue. The bronchial epithelium was lacking over the entire cartilage-deficient zone and was in the process of desquamating in many other places as well, which made it appear possible that the loss of cells was the result not of the acute inflammation which existed in the mucosa of the whole bronchus but of postmortem autolysis and desquamation. The inflammatory reaction was not marked, being limited to comparatively few

polymorphonuclear neutrophils. The blood vessels in the submucosa of the whole bronchus were abnormally prominent because of engorgement.

Sections of the upper lobe of the left lung displayed well defined dilatation of the air sacs, many of which were as large as are ever seen in cases of emphysema in adults. In spite of the dilatation, the majority of the blood vessels, both large and small, were well filled with erythrocytes. Many of the walls were fragmented and torn across. That some of this change occurred post mortem was attested by the fact that hemorrhage had not taken place into the alveoli, even though the ends of the divided capillaries were open. In other instances the ruptures appeared to be of longer standing, for the ends were sealed off, at least at the points of sectioning. There was no inflammation or edema. The vessels of the visceral pleura were distended. Sections of the lower lobe of this lung presented a picture very different from that just described, for here there were practically no open air sacs. The majority were collapsed, and those that were only partially so as a rule contained monocytes, sometimes with blood pigment but more often lacking any visible content. An occasional small bronchus contained polymorphonuclear leukocytes, and here and there these cells, alone or with mucus, filled the air sacs. Desquamation of the bronchial epithelium was a striking feature.

Sections taken from the left ventricle of the heart revealed no pathologic change. The liver and kidneys showed passive hyperemia.

COMMENT

In all available cases of similar deformities except that reported by Wethered, there was an anomaly of the bronchus which supplied the emphysematous portion of the lung. In Wethered's case the emphysema was attributed to disease of other portions of the lung, and he considered it compensatory. It is difficult to imagine that the elasticity of the lung could allow a bronchus to collapse in the absence of positive intrathoracic pressure. Such pressure might be applied by active expiration, such as that exerted by an infant in crying. Once such a process has allowed the affected portion to distend to the point of producing positive intrapleural pressure, compression may maintain the stenosis of the bronchus. Inspiration must always be the distending factor, and expiration, in the presence of a positive intrapleural pressure, the factor which maintains the emphysematous state of that portion of the lung until the limits of elasticity have been exceeded, at which time collapse may not occur. That the affected lobe maintained a fair amount of elasticity in the case reported here was demonstrated by its partial collapse when the thoracic cavity was opened. Figure 2, a photograph taken after inflation with a fixing agent, shows that while the upper lobe was tremendously dilated, it was not as large as indicated by the roentgenogram in figure 1.

In a similar case, occurring in another hospital, lobectomy failed to relieve the symptoms. At the time of the report the lung had not yet been dissected in search for a cause. The evidence in that instance was suggestive of a flap valve mechanism, as the excised lobe failed to collapse when moderate pressure was applied.

The cause for the enlargement of the right ventricle was not determined. Kountz and his co-workers [13] have demonstrated that generalized emphysema exerts its often tremendous increase in venous pressure outside the thoracic cavity and that circulation through the pulmonary circuit is not impeded. The effect is obstruction of the venous return at the entrance of the great vessels into the thorax, and right ventricular hypertrophy is not frequently observed with generalized emphysema. Torsion of the pulmonary artery and compression of the pulmonary bed through the remaining compressed lobes are probably factors accounting for the right ventricular hypertrophy in the case reported.

CONCLUSIONS

Lobar emphysema not associated with cystic disease of the lungs is unusual. The patient in this case was observed almost from the first manifestations of the condition. Although syphilis was present in the mother, the baby's early positive serologic reaction is best considered as due to passive transplacental transfer of the antibodies from the maternal circulation to that of the fetus, as evidenced by the absence of specific evidence of syphilis and by the fact that the reactions became negative without treatment. The anatomic abnormality was an unusually small bronchus, lacking in cartilage, in the upper lobe of the left lung.

13. Kountz, W. B.; Pearson, E. F., and Koenig, K. F.: Observations on Intrapleural Pressure and Its Influence on the Relative Circulation Rate in Emphysema, J. Clin. Investigation **11**:1281-1291 (Nov.) 1932.

DENTAL CARIES AMONG ESKIMOS OF THE KUSKOKWIM AREA OF ALASKA

I. CLINICAL AND BACTERIOLOGIC FINDINGS

THEODOR ROSEBURY, D.D.S.
AND
L. M. WAUGH, D.D.S.
NEW YORK

It is recognized, as a consistent result of the studies of many observers, that primitive peoples in widely scattered areas of the world are little subject to dental caries until they come into contact with civilized races and adopt some of their habits, when they suffer markedly increased incidence of decay. Such observations have been reported particularly of Eskimos,[1] and also of African natives,[2] New Zealand

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This paper is Unit 8, Section IV, of "Dental Studies of the Eskimos of North America," directed by L. M. Waugh, D.D.S., Consultant Dentist, Office of Indian Affairs, and Dental Director (Reserve) of the United States Public Health Service.

This work was made possible by a grant from the Office of Indian Affairs, United States Department of the Interior. The follow-up research was aided by a grant for dental research from the Carnegie Corporation. Dr. T. J. Pyle, Dental Director of the Indian Service in Alaska, gave help in the field; Mrs. L. A. Heron, nurse in charge of the dispensary at Bethel, gave help and advice at many points during the field work; Mrs. H. Oman, community worker at Eek and Quithluk, gave assistance in the field and dietary information concerning the Eek natives; Mr. C. Foster Jones, teacher at Kepnuk, furnished dietary information on that settlement; Mrs. Mary L. York, supervisor of the Moravian orphanage at Nunapitsinghak, gave information on the diet at the orphanage; Mr. Willard R. Olsen, trader at Bethel, supplied records of native trading, and Mr. Melvin Anderson gave laboratory assistance at Bethel and at Kokok.

Preliminary reports on this study were presented at the Fifteenth General Meeting of the International Association for Dental Research on March 13, 1937, and were published in the August 1937 issue of the *Journal of Dental Research*, pages 305-308.

1. (*a*) Mummery, J. R.: Tr. Odont. Soc. Great Britain **2**:7, 1870. (*b*) Leigh, R. W.: Dent. Cosmos **67**:884, 1925. (*c*) Waugh, L. M.: J. Dent. Research **8**: 428, 1928; **10**:387, 1930; **11**:453, 1931; **12**:426, 1932; J. Am. Dent. A. **24**:1640, 1937. (*d*) Rabinowitch, I. M.: Canad. M. A. J. **34**:487, 1936. (*e*) Krogh-Lund,

(Footnotes continued on next page)

Maoris,[3] Hawaiians,[4] Samoans,[5] Chinese[6] and a number of white peoples isolated from contact with the modern world.[7] There is general agreement, furthermore, that the factors responsible for the observed phenomena are principally, if not entirely, dietary, but attempts to go beyond this point to a more precise interpretation of the data have yielded only conflicting views, which collectively permit no judicious conclusion. For example, the characteristically high protein, high fat, low carbohydrate diet of the Eskimo, composed almost entirely of meat and fish, seems to have little in common with the diets of tropical races, in which abundant vegetables and fruit yield a relatively high carbohydrate content; yet both groups have little caries. Cereal grains, on the other hand, were rare among the people at Tristan da Cunha[7b] and common among primitive African races[2c] and the earlier inhabitants of the Valais district of Switzerland,[7d] but, again, all these areas were relatively free from caries. Abundance of fresh milk at Tristan da Cunha, according to Sprawson,[8] determined the natives' freedom from caries; but the Eskimos and the more primitive Samoans,[5] with equally sound teeth, had little or no milk other than human. Taro and sweet potatoes were held responsible for the sound teeth of the Hawaiians by Jones and her co-workers,[4] but abundance of the same foods at Pitcairn, according to Sprawson[8] was associated with rampant decay. Several of the primitive groups with little caries had diets rich in fresh vegetables

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G.: Lancet **2**:977, 1937. (*f*) Pedersen, P. O.: Dent. Rec. **58**:191, 1938; Tandlaegebladet **42**:127, 1938.

2. (*a*) Colyer, J. F.: Dental Surgery and Pathology, ed. 5, London, Longmans, Green & Company, 1923. (*b*) Orr, J. B., and Gilks, J. L.: Studies of Nutrition: The Physique and Health of Two African Tribes, Medical Research Council, Special Report Series, no. 155, London, His Majesty's Stationery Office, 1931. (*c*) Oranje, P.; Noriskin, J. N., and Osborn, T. W. B.: South African J. M. Sc. **1**:57, 1935.

3. Pickerill, H. P.: The Prevention of Dental Caries and Oral Sepsis, ed. 3, New York, Paul B. Hoeber, 1924.

4. Jones, M. R.; Larsen, N. P., and Pritchard, G. P.: Dent. Cosmos **72**:439, 574, 685 and 797, 1930; **76**:385, 1934.

5. Ferguson, R. A.: J. Am. Dent. A. **22**:392, 1935.

6. Anderson, B. G.: J. Dent. Research **12**:709, 1932. Montelius, G. A.: ibid. **13**:501, 1933.

7. (*a*) Carnegie Report on the Physical Welfare of Mothers and Children of Scotland (1913), cited by Mellanby, M.: Diet and the Teeth: An Experimental Study; III. The Effect of Diet on Dental Structure and Disease in Man, Medical Research Council, Special Report Series, no. 191, London, His Majesty's Stationery Office, 1934. (*b*) Sampson, W. E. A.: Dent. Surgeon **29**:219, 1932. (*c*) Barnes, H. N. V.: Brit. Dent. J. **63**:86, 1936. (*d*) Seiler, J.: Schweiz. Monatschr. f. Zahnh. **41**:489, 1931.

8. Sprawson, E.: Brit. M. J. **2**:516, 1932; Pub. Health Rep. **47**:388, 1934.

and fruit, and hence probably alkaline in potential reaction, but the Eskimos and the natives of the Island of Lewis (according to Jones [9]) apparently used a preponderance of acid-forming foods and had no more caries.

These apparent contradictions exemplify the complexity of the problem of dental caries. They may reflect fundamental differences in the nature of dental caries in different localities, but it is more likely that dental caries does not thus differ and that what is needed is a unifying principle, as yet unrecognized, which will lend the record a coherence it now appears to lack. If dental caries is the same disease wherever it occurs and if such a principle can be derived from a study of the disease in any one region, the principle should then apply without essential modification in all other localities.

The study of dental caries among an isolated people, including both primitive groups with little decay and less primitive groups with much, may consequently extend in importance beyond the needs of the particular people studied to embrace the problem as a whole, to which it appears to provide a promising avenue of approach. Such an investigation should deal with as primitive a group as possible, and with the primitive group should compare others of the same racial stock living under less primitive conditions. The study should proceed on a basis of sound clinical data, establishing the relative incidence of caries and the clinical nature of the disease, and should continue as a comparative study to collect all possible dietary records and other data that might have a bearing on the cause of the disease.

The first of these conditions was met in the present investigation, as a result of the earlier studies of Waugh [1c] and of Hrdlička.[10] According to Hrdlička: [10]

> The lower and middle parts of the Kuskokwim River . . . and the tundra region on both sides of it, are sparsely settled by what is still the largest and purest body of Eskimo, counting collectively about 3,000. These live in their own villages and occupy themselves mainly with trapping in winter, fishing in summer. Outside of some older Russian and a small amount of more recent American blood, they are unmixed. They are well preserved physically as well as morally, are self-supporting, and constitute not only the largest but in many respects the best existing Eskimo group for study.

The previous studies of Waugh and Waugh [11] had indicated that the primitive people in the Kuskokwim area are virtually free from caries while those living in or near white settlements suffer greatly from it, and had in other ways laid the foundation for the present study.

9. Jones, M. R.: J. Dent. Research **10**:281, 1930.

10. Hrdlička, A.: Am. J. Phys. Anthropol. **18**:93, 1933.

11. Waugh, L. M., and Waugh, D. B.: J. Dent. Research **15**:317, 1936.

The area under study in the present investigation, as indicated by the map (fig. 1), is part of the southwestern extremity of the Territory of Alaska, lying northwest of the base of the Alaska Peninsula. The lower part of the Kuskokwim River traverses the region, and many of the settlements from which the natives were drawn for our study are on or near the river. The region is remarkable in that it lies apart from the regular lanes of travel. There are neither roads nor railways in it;

Fig. 1.—Map showing the area under investigation.

commercial shipping between Nome and more southern ports does not enter the area, and only one commercial vessel and a government boat carrying school supplies make occasional visits to Bethel. Transportation into and within the region is carried on largely by airplane, supplemented by dog sleds in winter and by small boats in summer, the river and the adjoining coast being treacherous, with inadequately charted flats and shallows. The white settlements on the Kuskokwim River, of which Bethel, with a white population of 100 or less, is the largest, are peopled by missionaries, teachers, nurses and traders and their families.

with a few inhabitants who are engaged in mining operations in the hills lying east of the river. A considerable native population also inhabits these villages; in addition, the natives have their own villages, more or less removed from white contact, on both banks of the Kuskokwim River and in the tundra area west of the river and extending to the coast of the Bering Sea. Many natives of the coast and the tundra, as well as those from Nelson and Nunivak Islands, migrate to points along the west bank of the Kuskokwim River for summer fishing and thus become easily accessible by small boat from Bethel.

Four objectives were planned for this investigation in accordance with the conditions previously mentioned: (*a*) to make bacteriologic studies and (*b*) to carry out chemical analyses of the saliva of natives free from caries and of natives having active caries, both for comparison of the results obtained with those previously found among white peoples, as an index of the nature of the disease among the Eskimos, and as a check on the previous findings under the different conditions obtaining in the field; (*c*) to collect clinical data on caries and associated oral conditions for all native subjects used in the bacteriologic and chemical studies, in order to permit adequate classification of cases by methods previously employed and as a further check on the nature of caries among Eskimos, and (*d*) to gather data on the dietary habits of the primitive and the less primitive native groups and to collect samples of native foods for chemical analysis, in a manner to be determined by conditions in the field. This report includes the first and third of these phases of the investigation. The others are discussed in separate reports.

GENERAL METHODS

Facilities for the transportation of freight into the area being limited, the laboratory work in the field was planned and conducted so as to utilize a minimum of heavy equipment. A small kerosene incubator had been transported to Bethel the previous summer. Most of the additional equipment was forwarded via the *M. S. Tupper*, which entered Bethel on one of its regular trips early in June 1936. Other materials, which could not be made ready in time to be put aboard the *Tupper*, were carried by freight to Anchorage, Alaska, and thence by plane. There were included a small copper oven with a water jacket for drying samples of food, a water still comprising a brass Liebig condenser and glass flasks, a microscope, a heavy welded iron box with a loose-fitting overlapping cover for sterilization of pipets by dry heat and a large fish kettle for washing and sterilizing glassware by boiling. As much as possible of the chemical glassware was washed before packing and was packed clean; the remainder was washed at the field laboratory, a cleaning mixture of sodium bichromate and sulfuric acid in distilled water being used. Glassware for bacteriologic work was packed sterile, but in the field facilities for washing and sterilizing both Petri dishes and pipets were adequate. Agar and clear broth mediums were shipped in 12 ounce (355 cc.) bottles of the type formerly used for dispensing magnesium citrate, with porcelain spring tops covered with paper and clamped down after autoclaving. Chopped meat broth was packed in Noguchi tubes (1 by 30 cm.), which were sealed in a flame after being autoclaved.

Sterilized cotton plugs to fit these tubes were wrapped separately, and the tubes were cut and plugged before use. All necessary stains, reagents, instruments, tools and other accessories were included. Further details of individual methods will be given in later sections of this paper and in the succeeding papers.

The field work was done between June 17 and Aug. 20, 1936, chiefly at Bethel, where the base laboratory was set up. Several trips were made to outlying areas: to Bethel Island, to the Moravian orphanage at Nunapitsinghak, to Napakiak and to Eek, Pepok and several Kokok fish camps, at one of which a temporary laboratory was set up.

CLINICAL STUDY

Selection of Subjects.—Only subjects were used who seemed to be full blood Eskimos, as determined by their appearance and by the advice of white inhabitants who knew them, when this was available. Some degree of racial admixture may have been present among these natives, but it was probably both infrequent and several generations removed, since more recent admixture is not difficult to detect. Among the earlier subjects no other basis for selection was imposed. Most of these were inhabitants of Bethel or of settlements in its vicinity and had caries. Beginning with the Napakiak group and in all subsequent groups subjects free from caries or those with active caries or both were selected, in order that the best use might be made of the limited supply of culture mediums. As a result of this selection, the values obtained for the incidence of caries in the different localities are not beyond question, particularly since the individual geographic groups are small. Nevertheless, in all areas except Napakiak, where only subjects free from caries were chosen, both types were selected, the number of each depending on the relative availability of the two types in the area. The values, moreover, are in line with the experience of white residents of several of the communities, who are familiar through close contact with conditions among the natives. The data are therefore offered with little doubt that their relative accuracy is sufficient for the purposes of this study.

Examination of the Mouth and Case Routine.—Although the mouths had to be examined without elaborate equipment, usually in the open air, care was taken to be as thorough as conditions permitted and to record the findings systematically and in full. To meet the requirements of the bacteriologic and chemical studies, intensive examination of a relatively small group seemed preferable to a more cursory but extensive survey, which might have been more suited to the dietary study. The examinations were made with a mouth mirror and explorer and with a chip blower and floss when necessary. The location and the approximate size of all carious lesions were charted, and an attempt was made to define the relative penetrability of the lesions: All areas in which the condition seemed uncertain for any reason, such as deep fissures or stained areas with no clear evidence of softening or cavities with hardened dentin in which the process appeared to be arrested, were recorded as doubtful. The presence of one or more such areas excluded a subject from the group free from caries and, unless the defect was accompanied by apparently active (that is, soft) lesions, from the group with active caries as well. Fillings and missing or unerupted teeth were recorded. Irregularities of alinement of the teeth and hypoplasia of enamel were noted as present or absent. Attrition was recorded by degree according to the classification described by Leigh.[1b] Salivary calculus was indicated as follows: absent, 0; slight deposits limited to the lingual surfaces of the lower anterior teeth, to the buccal surfaces of the upper molars or to both, ±; moderate deposits limited for the most part to the same areas, +, and more extensive deposits on many or all teeth, + +.

The subject's name and village of origin were recorded on the charts, with his approximate age. The children of Bethel and vicinity and many of those seen at Kokok were known to Mrs. Heron and those of Eek to Mrs. Oman, and their exact ages were thus available; but since the Eskimos themselves can provide no accurate information on this point, the ages of others, in particular of adults, were a matter for conjecture and were recorded as estimates.

After the clinical examination the subject was given paraffin and instructed to chew and to spit into a sterile plugged test tube, graduated to 10 cc., for about three minutes. Immediately thereafter, when conditions permitted, the subject continued to chew, and about 15 cc. of saliva was collected in a second tube. A period of rest was then allowed, which under field conditions could not be well controlled but ranged from about five to fifteen minutes, after which the subject chewed a new paraffin pellet and an additional amount of about 8 cc. of saliva was collected in a third tube. All tubes were labeled with a diamond pencil. The first specimen was used for the bacteriologic study; the others, for chemical analysis, were treated at once with mercury bichloride, 0.05 cc. of a 2 per cent aqueous solution being added to each by pipet and stirred well and the tubes being closed with rubber stoppers. The basis for this procedure and other details of these methods are given in the succeeding report.

No attempt was made to obtain information from the individual subjects on their diets or in other ways to amplify or depart from the routine described. Not only did such information seem of doubtful validity, but under the rather difficult field conditions constant vigilance and care were required to follow the routine adequately, without additions.

Clinical Data.—The clinical study comprised 124 native subjects, of which 106 (excluding those at the orphanage) were used for the bacteriologic study and 49 for the chemical study. The subjects were classified clinically into three groups: (*a*) those with caries, who had two or more well developed cavities with softened dentin; (*b*) those free from caries, who had all their teeth (present or obviously unerupted), with neither cavities nor doubtful areas, and no fillings, and (*c*) those with doubtful caries, comprising all subjects not included in the preceding groups, such as those with occlusal pits only, those with apparently nonprogressive (hard) cavities or with only one soft cavity and those without caries but with one or more missing teeth. As a basis for selection of subjects with active caries, softened dentin was preferred to chalky enamel, such as occurs in early active proximal caries, since the latter was comparatively uncommon among these people.

The clinical data are summarized in tables 1 to 5. Table 1 gives the geographic distribution of carious, filled and missing teeth. Natives from Bethel, from the white settlements north of Bethel and from the native villages in the tundra west of Bethel showed the highest incidence of carious teeth and affected dental surfaces. The natives of this group live in relatively close association with the white man. On the other hand, natives from the more primitive villages on the coast of the Bering Sea, most of whom were seen at Kokok and adjoining fish camps, had the lowest incidence of caries. The values, although subject to error of sampling previously remarked, are believed to reflect with sufficient fidelity the striking difference in dental condition between these two groups which even a cursory examination of these people cannot fail to

reveal. This finding is in agreement with previous observations among both these and other Eskimos and among primitive peoples generally, as noted earlier.

The three other groups recorded in table 1 are of particular interest. Eek is an isolated primitive community situated east of the Kuskokwim River near its mouth, on a tributary, the Eek River. The Eek people have little contact with Bethel and do not mingle with the natives that inhabit the summer settlements on the adjacent west bank of the Kuskokwim River. Eek is itself a native village, not a white settlement, but it has a resident white trader and, in addition, a white teacher-nurse, who with their families comprised the entire white population. Despite this limited degree of contact with the influence of the white

TABLE 1.—*Distribution of Carious Teeth, Fillings and Missing Teeth Among Kuskokwim Eskimos from Different Regions*

Region	Number	Average Age, Yr.	Average Number Carious Teeth per Person	Average Number Fillings per Person	Average Number Missing Teeth per Person	Carious Teeth, Percentage*	Carious, Filled or Missing Surfaces, Percentage*
Bethel and vicinity†	47	16.3	5.03	0.26	1.28	22.9	10.02
Eek	20	18.4	4.35	0	0.15	18.1	6.96
Orphanage	18	15.3	2.72	0.78	0.33	10.0	3.71
Primitive villages‡	39	21.7	0.49	0	0.13	1.6	0.55
Kepnuk§	9	21.6	0.33	0	0	1.2	0.23

* The percentage values are averages of individual percentages based on the number of teeth and on the number of dental surfaces in the mouth, respectively.

† This includes Quithluk, Akiak, Kalskag and the tundra villages west of Bethel.

‡ This includes Napakiak, Quigillingnok, Kepnuk, Nelson Island, Nunivak Island and other coastal villages.

§ The data on Kepnuk are given separately with reference to the dietary study.

race, the Eek people have nearly as much caries as those of Bethel. The comparative simplicity of these conditions suggested the value of Eek as a subject for the dietary study; further details in this connection will be given in the third report of this series.

The Moravian orphanage at Nunapitsinghak, about 18 miles (29 kilometers) above Bethel, lying on a slough (the Kuskokwok) to the east of the Kuskokwim River, is also of interest, chiefly in connection with the dietary study, and as such is described in greater detail elsewhere. Clinical data for the orphanage are given in table 1 but not in tables 2 to 5, since the natives in the orphanage were not used for the bacteriologic or chemical studies. The subjects studied at the orphanage represent most of the native population; a somewhat smaller number of "breeds" were not included. The incidence of caries, it will be noted, was intermediate between that at Bethel or at Eek and that at the primitive villages. The orphans receive some dental attention from the Indian Service, as do some of the children at Bethel.

unlike the other groups. The children of the orphanage alone are taught to brush their teeth regularly and have clean mouths.

The small group of Kepnuk natives has been separated from the other primitive groups in table 1, again for comparison in relation to the dietary study. It will be noted that this group, although small, is representative of the primitive group generally; the somewhat lower values for the Kepnuk group as compared with those for the whole

TABLE 2.—*Distribution of Cavities According to Location on the Surfaces of the Teeth* *

	Deciduous						Permanent					
	Active		Inactive		Pits		Active		Inactive		Pits	
Surface	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Occlusal	37	20.7	4	2.2	5	2.8	132	46.3	6	2.1	65	22.8
Proximal	96	53.6	16	8.9	..	...	37	13.0	6	2.1	..	....
Buccal	2	1.1	..	...	..	...	2	0.7	6	2.1	20	7.0
Cervical	..	....	..	...	..	...	3	1.1	..	...	..	....
Compound	15	8.4	4	2.2	..	...	6	2.1	2	0.7	..	....

* Percentages are given separately in terms of the total number of cavities in deciduous teeth (179) and in permanent teeth (285).

TABLE 3.—*Distribution of Carious Teeth According to Location of Teeth in the Mouth* *

	Deciduous				Permanent			
	Upper		Lower		Upper		Lower	
Tooth	No.	%	No.	%	No.	%	No.	%
1st incisor	10	62.5	0	0	7	7.5	3	3.1
2d incisor	8	50.0	0	0	8	8.8	1	1.1
Canine	13	44.3	7	26.9	2	2.8	1	1.2
1st premolar	..	....	..	....	9	11.3	3	3.8
2d premolar	..	....	..	....	10	13.3	5	6.6
1st molar	23	74.2	22	75.9	44	44.0	47	48.5
2d molar	25	78.2	16	59.3	27	41.6	43	61.5
3d molar	..	....	..	....	11	33.3	10	35.1

* Percentages are given in terms of the total number of teeth of each type examined.

primitive group are consistent with the fact that Kepnuk is known to be one of the most primitive of the villages.

The character of the individual lesions of dental caries seen among these peoples is clinically indistinguishable from that of carious lesions among white people. Tables 2 and 3 summarize the distribution of caries according to location on the teeth and in the mouth. These distributions will be seen to correspond generally with the usual picture, with certain exceptions. Table 2 indicates that proximal cavities preponderate in the deciduous teeth, while occlusal cavities are much more common than any other variety in the permanent teeth. Together, occlusal and proximal cavities, in both deciduous and permanent teeth, constitute nearly the whole distribution. The comparative rarity of

other types is in interesting accord with the finding, to be noted, that caries among these people is a disease of children and young persons in even greater degree of preponderance than among white peoples. The occlusal and proximal varieties of caries are, of course, the more characteristic of younger age groups in general experience. The distribution of lesions by location or type of tooth (table 3) indicates a typical or customary picture.

In table 4 the data for the three groups classified according to activity of caries are presented and compared in regard to the respective incidence of the other oral conditions recorded. The number of fillings found was negligible, since most of these people receive no dental treatment; the low incidence of missing teeth is therefore the more

TABLE 4.—*Relation of Dental Caries to Other Clinical Findings*

Condition of Teeth*	Number of Subjects	Males	Females	Average Age, Yr.	Average Percentage of Carious Teeth	Average Number of Cavities per Person	Average Number of Missing Teeth per Person	Average Number of Fillings per Person	Attrition		Salivary Calculus		Hypoplasia of Enamel, Incidence, Percentage	Irregularity of Alinement, Incidence, Percentage
									1 Degree or More, Percentage	Average Degree	Incidence, Percentage	Average Degree †		
Caries	36	23	13	14.0	35.1	7.6	1.0	0.3	16.7	0.3	25.0	0.2	5.6	11.1
No caries	44	30	14	27.7	0	0	0	0	66.0	1.3	88.6	1.0	2.3	15.9
Doubtful caries	26	14	12	21.1	9.2	3.3	0.5	0	50.0	0.7	57.7	0.6	0	19.2

* Subjects with caries had two or more well developed soft cavities; subjects free from caries had no evidence of caries, no fillings and no extracted or lost teeth; subjects with doubtful caries had enamel pits only, apparently nonprogressive (hard) caries, only 1 soft cavity or no evidence of caries but one or more extracted or lost teeth.

† Calculated on the basis that ± indicates 0.5, +, 1 and ++, 2.

remarkable, indicating the relatively recent origin of caries among these Eskimos, as noted more fully later. The values for hypoplasia of the enamel and irregularity of alinement indicate that neither condition is common but suggest that neither can be correlated with caries. On the other hand, attrition and salivary calculus are both much less common in the group with caries than in the group free from caries. The group with doubtful caries generally presents intermediate values, as would be expected.

It is further noteworthy that the group with caries and the group free from caries differed considerably in average age, as indicated in table 4. In Table 5 the data are classified by age groups, subdivided arbitrarily so as to be approximately equal in size. The expected increase, with advancing age, in incidence and degree of both salivary calculus and attrition is clearly indicated, whereas a corresponding

decrease in caries appears. Some of the data in table 5 are shown graphically in figure 2, in which the curves indicate the trends in deposition of calculus, attrition and caries with advancing age. The labeled points in figure 2 are derived from the data in table 4: The highest point is the value 88.6 per cent for the incidence of calculus in the group free from caries, plotted against the average age of the group, 27.7 years; the other points correspond for the group with caries, the group free from caries and the group with doubtful caries for both calculus and attrition. The fact that the three points for attrition fall close to the age curve suggests that the apparent inverse relation between caries and attrition depends entirely on the age differ-

TABLE 5.—*Data on Dental Caries and Other Oral Conditions Classified According to Age*

Age Range, Yr.	Average Age, Yr.*	Number of Subjects	Number with Caries	Percentage with Caries	Average Percentage of Carious Teeth	Average Number of Cavities per Person	Average Number of Missing Teeth per Person	Average Number of Fillings per Person	Attrition		Salivary Calculus		Hypoplasia of Enamel, Incidence, Percentage	Irregularity of Alinement, Incidence, Percentage
									1 Degree or More, Percentage	Average Degree	Incidence, Percentage	Average Degree †		
3-9	7.4	23	17	73.9	29.4	8.7	0.04	0.13	13.0‡	0.3‡	17.4	0.3	8.7	4.4
10-17	13.5	26	19	73.1	20.0	6.2	0.42	0.23	15.4	0.2	57.7	0.6	3.8	11.5
18-27	20.8	29	15	51.7	8.6	3.1	0.21	0.07	44.8	0.5	65.5	0.7	0	17.3
30-70*	44.1	28	6	21.4	2.5	0.8	1.14	0	100.0	2.2	89.3	0.8	0	3.6

* All ages are approximations based on available information; ages are most uncertain in the oldest group.
† Calculated on the basis that ± indicates 0.5, +, 1 and ++, 2.
‡ Attrition of deciduous teeth; no attrition of permanent teeth was observed in this group.

ential of the groups. On the other hand, by the same reasoning, the location of the points for calculus shows that the incidence of calculus in the group with caries was much lower than would be expected from the average age of this group according to the data in table 5 and, conversely, that the incidence of calculus in the group free from caries was considerably higher than its average age would have warranted. Analysis of these data by the chi square technic,[12] employing the age grouping of table 5 and the three classes of caries and the attrition and calculus classifications of table 4, yields the following results: The distribution of attrition among the age-caries classes, based on assumed independence of caries and attrition in each age group, is approximately normal; the deviations observed are such as would occur in random

12. This analysis was supplied by Prof. Earle B. Phelps, of the Delamar Institute of Public Health, Columbia University.

sampling about once in three trials. On the other hand, the corresponding distribution of calculus departs from the normal to a degree that would occur in random sampling less than once in a hundred trials, which indicates a high and significant probability against the assumption of independence. The data thus provide no significant evidence of a true relation between caries and attrition except by the incidental age relation. Neither do they support the opposite view of strict independence. They strongly support the conclusion that caries and salivary

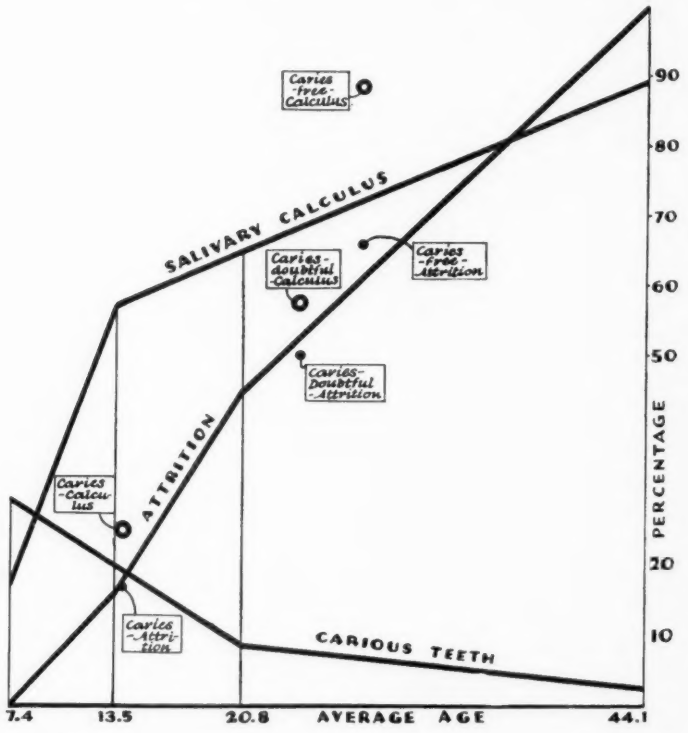

Fig. 2.—Chart showing the relation of age to the incidence of dental caries, attrition and salivary calculus and the relation of attrition and salivary calculus to dental caries among Alaskan Eskimos.

calculus are inversely related, per se, and are independent of the associated age relation.

The decrease of caries with increasing age shown in table 5 is itself a striking finding. The effects of caries are cumulative, and in groups in which the disease has been present continuously for several generations would be progressively augmented with advancing age or would lead to a marked increase of missing teeth or of fillings or other replacements. The data in table 5 indicate the rarity of fillings among

the Eskimos; other replacements are of course lacking, and the irregular slight increase in missing teeth, at most virtually negligible, does not compensate for the distinct and progressive decrease of caries from the youngest group to the oldest. These findings seem to point strongly to the conclusion that dental caries is of comparatively recent origin among these Eskimos. At all events, they indicate that a generation ago, when the older natives now alive were children, the disease was much less prevalent.

Data on a few individual subjects will be presented for their value in exemplifying and illustrating the data in the tables. Among the cases of active caries the following, including 1 from each age group, seem worthy of individual notice:

REPORT OF CASES

I. T., a 7 year old boy of Quithluk, had the most severe dental caries observed, the condition being present in every tooth except the 4 lower deciduous incisors. The 4 first permanent molars had erupted, and each had a small occlusal cavity. The deciduous teeth were all present except the lower left second molar, which had been extracted. The upper right second molar had a small occlusal cavity and a large mesial cavity; the upper left second molar had 2 similar cavities and, in addition, a moderately extensive buccal cavity. All the intervening upper deciduous teeth had well developed cavities, both mesial and distal. The lower right first and second deciduous molars were decayed nearly to the gingival line; both canines had large distal cavities, and the lower left first molar had well developed cavities, both mesial and distal. This represented a total of 31 cavities, affecting 82.5 per cent of the teeth. I's two brothers, W., aged 9, and G., aged 11, also had extensive caries; the former had 10 cavities in 40 per cent of his teeth and the latter 18 cavities in 54.6 per cent of his teeth. The lower values for the two older brothers were probably due to exfoliation of deciduous teeth (all of those remaining being carious) and to recent eruption of permanent incisors and (in G's mouth) of the premolars and the canine on the lower left side, the newly erupted permanent teeth (except the molars) being noncarious.

M. T. W., a 15 year old girl of Eek, had her permanent dentition, the third molars being unerupted and the lower right first molar missing. The upper left first molar, the lower left first molar and the lower right second molar were decayed to the gingival line. Occlusal cavities were present in the upper right first and second and upper left second molars, in both upper first premolars and in the lower right first premolar. The upper right second incisor had a gingival cavity, the upper left first incisor a distal cavity and the upper left second incisor a lingual cavity. There were 13 cavities in all, affecting 48.2 per cent of the teeth. The upper canines had erupted labially to the arch.

A. L., a 20 year old man of Akiak, had all his permanent teeth in place except the upper left third molar, which was unerupted; the lower third molars were partly erupted. On the upper right side the second molar had a large occlusal cavity and the first molar and the second premolar a mesial and a distal cavity, respectively. On the upper left side the first premolar had a large distal cavity; the second premolar was decayed to the gingival line; the first molar had a large mesial and a small distal cavity, and the second molar had a large mesial and a

small occlusal cavity. On the lower left side the second molar had small buccal, occlusal and mesial cavities; the first molar had well developed distal and mesial cavities, and the second premolar had a distal cavity. On the lower right side the second premolar and the first molar had small distal and mesial cavities, respectively; the first molar also had a large occlusobuccal cavity; the entire occlusal surface of the second molar was carious. There were 19 cavities, affecting 43.3 per cent of the teeth. The upper second incisors had erupted lingually, and the upper right canine had erupted labially, to the arch.

I. H., a 45 year old man, of Kalskag, was the only subject over 26 years old with more than 3 cavities. The upper right third molar, lower right first molar and lower left second and third molars had been lost. Five teeth were decayed to the gingival line: the upper right second molar, the upper left first and second molars, the lower left first molar and the lower right third molar. Small proximal areas on both teeth at the contact between the upper first molar and the second premolar on the right were recorded as doubtful caries. There were small cavities mesially and distally on the upper right first incisor and mesially on the upper left first incisor. There were 10 cavities in all, affecting 25 per cent of the teeth. Slight deposits of calculus appeared on the lower incisors only, recorded as ±. There was first degree attrition.

Among the subjects free from caries, although they appeared in all the age groups, the younger ones presented little that was of individual interest. There were many subjects who showed the following pattern with minor variations, the example being chosen at random:

T., a 14 year old boy of Napakiak, had a complete set of permanent teeth but for the third molars, which were unerupted. He had no caries; moderate deposits of calculus were noted labially and lingually on the lower anterior teeth and buccally on the upper molars (+), and first degree attrition was present.

Of the oldest subjects, however, 2 that presented interesting individual features may be described:

K., a woman of Eek, clearly the oldest of all the subjects, was of indeterminate age, which was variously estimated to be from 70 to 80 years and recorded conservatively at the lower figure. She was a great grandmother, her granddaughter's age being estimated at 45. K. had all 32 permanent teeth in place, with no evidence of caries. She had fourth degree attrition, all of her teeth being worn nearly to the gingival line, with exposure of the pulp chambers. Many areas of chipped enamel were present particularly at contacts, a condition characteristic of many of the older primitive natives. She had little calculus (±) and no apparent periodontal or gingival disease.

Ts., a woman of Bethel aged about 65 years, presented a picture somewhat similar to that just described. She had all 32 permanent teeth without caries. There were third degree attrition of the posterior teeth and advanced fourth degree attrition of the anterior teeth; the entire crowns had been worn away so that, evidently through loss of the normal contacts, a space of about ¼ inch (0.64 cm.) intervened between the worn stumps of the upper central incisors. These were firm, however, and evidently still in active service. Heavy localized deposits of calculus occurred lingually on the upper incisors; otherwise there were only slight deposits. The upper left first molar had evidently lost most of its bony attachment, being loose and somewhat painful.

An opportunity was provided to make roentgenograms of Ts. and several other subjects in Bethel. Some of these, taken as improvised bite wing photographs, are given in figures 3 and 4. Figure 3 *A* is

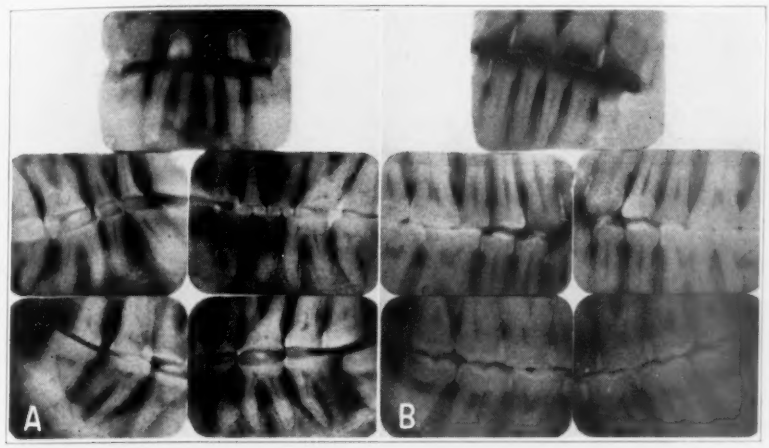

Fig. 3.—Intraoral bite wing roentgenograms. *A*, teeth of Ts., a Bethel Eskimo woman aged about 65. See the text for a description of this subject. *B*, teeth of N. C., a Quithluk Eskimo man aged 30. The buccal wall of the upper left third molar was fractured. Small occlusal cavities were present in the upper left second molar and the lower left third molar.

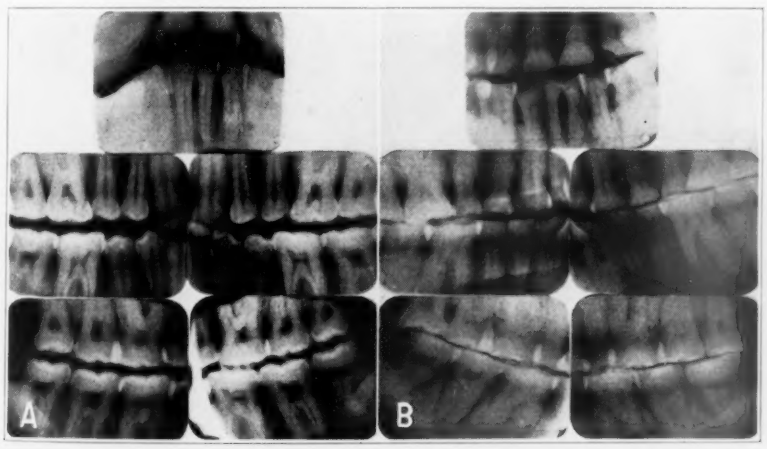

Fig. 4.—Intraoral bite wing roentgenograms. *A*, teeth of H. J., a Napakiak Eskimo man aged 20. All were present, and there was no caries. Note the bilateral symmetry of the dental structures. *B*, teeth of K. C., a Bethel Eskimo woman aged about 50. All were present, with third degree attrition and no caries.

that of Ts. Attention may be directed to the remarkable bilateral symmetry shown in figure 4 *A*, which may be taken as suggestive of the dental perfection of the Eskimos.

BACTERIOLOGIC STUDY

The search by laboratory means for differences between groups of persons free from caries and those with active decay has, naturally, been one of the most promising methods of attack on the problem of the etiologic factors in the disease. Among the findings in this field certain bacteriologic data have been most striking. Building on the earlier investigations of Kligler and Gies [13] and others,[14] Bunting and his collaborators [15] have been especially active in developing this subject. These findings have been discussed in greater detail elsewhere.[16] The essential finding was a positive correlation in high degree between the occurrence of lactobacilli on the teeth or in the mouth at large, both qualitatively and quantitatively, and the activity of dental caries. In the mouths of persons with active dental caries, these bacteria occur regularly and in large numbers; in mouths free from decay they occur relatively infrequently, and when present their numbers are generally small. Lactobacilli as a class are notable for their capacity both to produce and to withstand relatively high concentrations of acidity resulting from fermentation of carbohydrates, and their correlation with activity of caries consequently accords with Miller's [17] generally accepted theory of the mechanism of the disease. This and other circumstantial evidence [18] points to the probable importance of lactobacilli as inciting agents of dental caries.

One of the objects of the present study was to check the findings of Bunting and his co-workers, particularly as to their quantitative aspects. Eskimo groups seemed to offer ideal conditions for the purpose, since they provide persons free from caries both in much greater relative abundance and with greater presumptive reliability (because of their long history of freedom from caries) than do less primitive groups. Conversely, the study was expected to throw addi-

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14. Howe, P. R., and Hatch, R. E.: J. M. Research **36**:481, 1917. McIntosh, J.; James, W. W., and Lazarus-Barlow, P.: Brit. J. Exper. Path. **3**:138, 1922. Rodriguez, F. E.: Mil. Dent. J. **4**:199, 1922.

15. (*a*) Bunting, R. W., and Palmerlee, F.: J. Am. Dent. A. **12**:381, 1925. (*b*) Bunting, R. W.; Nickerson, G., and Hard, D. G.: Dent. Cosmos **68**:931, 1926. (*c*) Bunting, R. W.; Nickerson, G.; Hard, D. G., and Crowley, M.: ibid. **70**:1, 1928. (*d*) Jay, P., and Voorhees, R. S.: ibid. **69**:977, 1927. (*e*) Jay, P.; Hadley, F. P.; Bunting, R. W., and Koehne, M.: J. Am. Dent. A. **23**:846, 1936.

16. Rosebury, T., in Gordon, S. M.: Dental Science and Dental Art, Philadelphia, Lea & Febiger, 1938.

17. Miller, W. D.: The Micro-Organisms of the Human Mouth, Philadelphia, S. S. White Dental Mfg. Co., 1890.

18. Rosebury, T.: J. Bact. **24**:321, 1934. Canby, C. P., and Bernier, J. L.: J. Am. Dent. A. **23**:2093, 1936.

tional light on the relation of dental caries as a disease among Eskimos to dental caries as it is known among other peoples.

A preliminary bacteriologic study in the area of the present investigation, conducted during the summer of 1935 by Waugh and Waugh,[11] suggested a confirmation of previous qualitative findings. Otherwise, to our knowledge, no comparable study among Eskimos or any other primitive people has been reported on in detail.[19]

Methods.—Tomato agar was prepared according to Hadley's [20] modification of the formula of Kulp and White,[21] except that Difco neopeptone was used instead of ordinary peptone. The medium was titrated by means of the glass electrode; after being autoclaved it had a final p_H of 4.99. Chopped-meat broth containing 1 per cent of dextrose, as used for this purpose by Thompson [22] and by Greenberg and Rosebury,[23] was prepared in two batches, the p_H being 4.7 and 3.8, respectively.

Bacteriologic analysis for the aciduric flora was made of the first specimen of saliva, as previously noted, which had been collected in sterile plugged tubes graduated to 10 cc. during approximately three minutes of stimulation by chewing paraffin. The saliva, made up to 10 cc. with sterile saline solution, was plated by the quantitative method of Hadley,[20] which was used without essential modification, except that the tomato agar plates were incubated for four days instead of three, at the suggestion of Jay.[24] Inoculations were always made on the day of collection of saliva. Two or more dilutions of each sample of saliva were plated by surface streaking, the quantities being adjusted as recommended by Hadley. One cubic centimeter of the original sample of saliva as diluted to 10 cc. was introduced by pipet into each of the chopped meat mediums in most instances, while the supply of these tubes lasted, as a qualitative check on the Hadley method.

After incubation the types of the colonies on the plates were distinguished morphologically and by Gram-stained smears, and Gram stains were made of the chopped meat broth cultures. Since the number of types cultivable on the acid mediums employed is limited, adequate generic differentiation was practicable on the morphologic basis alone, and a satisfactory differential count could be made directly from the plates. Gram-positive rods, obtained from colonies varying in size from that of a pinpoint to a diameter of about 3 mm. and in form from rough to smooth, were identified as lactobacilli. Cocci were distinguished by similar means as staphylococci, sarcinae, micrococci or gaffkyae. Including yeasts, virtually all the forms seen could be placed readily in one of these categories. There were 3 exceptions: a streptococcus in 2 instances, and a gram-negative bacillus in 1. The smears from chopped meat broth were examined for the presence of gram-positive rods, yeasts and cocci, the last without further differentiation.

An opportunity was provided to compare our tomato agar with a batch prepared in the laboratory of the "Michigan group" (Bunting,[15] Jay,[24] Hadley [20]) at Ann Arbor and furnished by Dr. Philip Jay. Samples from 7 of the earlier subjects were studied in parallel with the two mediums. The results, given in table 6,

19. An abstract alluding without details to a study of lactobacilli among Mayan Indians was recently published (Hill, T. J.: J. Dent. Research **16**:346, 1937).

20. Hadley, F. P.: J. Dent. Research **13**:415, 1933.

21. Kulp, W., and White, V.: Science **76**:17, 1932.

22. Thompson, R.: Proc. Soc. Exper. Biol. & Med. **29**:103, 1931.

23. Greenberg, S., and Rosebury, T.: J. Dent. Research **13**:236, 1933.

24. Jay, P.: Personal communication to the authors, 1936.

indicate a close correspondence, particularly with respect to lactobacilli, which were similar in both form and number on the plates from all but 1 of the subjects. Differences in numbers of the other types are to be accounted for partly by the fact that only small absolute numbers appeared on the plates (1,000 yeast organisms per cubic centimeter, for example, representing only 5 colonies on the plate with a dilution of 1:20, inoculated with 0.1 cc.), but the greater incidence of cocci on the plates prepared with our own agar suggests that its content of neopeptone may have made it more nutrient for these organisms.

Bacteriologic Data.—All of the 106 subjects described clinically in the preceding section were studied bacteriologically by the Hadley method; the chopped meat broth with a p_H of 4.7 was used for 88 of these, and the broth with a p_H of 3.8 for 85. The results are summarized in tables 7 and 8, in both of which the grouping according to caries is that previously described.

TABLE 6.—*Results of Control Test on Seven Samples of Saliva Plated with Uniform Technic on Two Preparations of Tomato Agar* **

Subject	Dilution	Lactobacilli		Micrococci or Gaffkyae		Yeasts	
		A	B	A	B	A	B
M. J.	1:20	0	0	0	0	1,200†	1,200†
	1:5	0	0	0	0	450	0
A. W.	1:20						
	1:5	All plates sterile					
I. H.	1:20	46,600‡§	59,800‡§	600§	2,800§	0	0
	1:5	43,500‡§	46,400‡§	0	0	0	0
O. E. J.	1:20	0	0	1,200	0	600§	400§
	1:5	0	0	150	0	350	0
M. J.	1:20	153,400‡§	173,800‡§	0	0	1,000†	800†
	1:5	214,500‡§	161,500‡§	0	0	100†	350†
F. I.	1:20	400§‖	200§‖	400	0	0	400
	1:5	150§‖	300§‖	8,750	0	150†	250†
J. S.	1:20	3,200¶	7,800#	0	0	0	0
	1:5	30,450¶	7,850#	23,250	0	0	0

* The tomato agar had a p_H of 5. Type A was prepared by us and type B by Dr. Philip Jay.
† More mucoid and slightly larger on A.
‡ Rough, flat, less than 2 mm. in diameter.
§ Similar on A and B.
‖ Smooth, raised; up to 3 mm. in diameter.
¶ Small rough colonies only.
# Both rough and smooth forms.

Table 7 presents the results qualitatively, as the incidence of positive cultures of the different generic types of aciduric bacteria obtained, given for the three mediums separately and in combination. It will be observed that material from 17 of the 44 subjects free from caries, or 38.6 per cent, yielded no growth with any medium, whereas that from only 3 of 36 subjects with active caries, or 8.3 per cent, yielded sterile cultures. This relationship appears in each of the individual mediums, cultures of the group with doubtful caries occupying the expected intermediate position. It is evident that this finding depends largely on the lactobacilli, which showed a striking direct correlation with activity of caries in all mediums. Cultures of only 6 of the subjects

without caries, or 13.6 per cent, yielded lactobacilli, whereas these bacteria were obtained in one or more of the mediums from 29 of the subjects with caries, or 80.6 per cent. Again, the cultures of

TABLE 7.—*Incidence of Aciduric Bacteria in the Mouths of Eskimos Correlated with Activity of Dental Caries* *

Type of Culture	Condition of Teeth	Number Studied	Cultures Sterile		Positive Cultures: Lactobacilli		Yeasts		Micrococci or Gaffkyae		Staphylococci		Sarcinae		Other Forms	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Tomato agar, p_H 5	Caries	36	7	19.4	25	69.5	11	30.5	8	22.2	5	13.9	3	8.3	0	0
	No caries	44	20	45.5	6	13.6	1	2.3	11	25.0	14	31.8	2	4.6	1†	2.3
	Doubtful caries	26	9	34.6	8	30.8	5	19.2	11	42.3	3	11.5	1	3.9	1‡	3.9
											Cocci, Undifferentiated					
Chopped meat broth p_H 4.7	Caries	36	5	13.9	26	72.3	5	13.9	..	....	11	30.5				
	No caries	32	22	68.8	1	3.1	0	0	..	....	9	28.1				
	Doubtful caries	20	4	20.0	7	35.0	3	15.0	..	....	13	65.0				
Chopped meat broth p_H 3.8	Caries	30	20	66.7	10	33.3	4	13.3	..	....	1	3.3				
	No caries	36	31	86.1	1	2.8	0	0	..	....	4	11.1				
	Doubtful caries	19	13	68.5	2	10.9	1	5.3	..	....	3	15.8				
All mediums combined	Caries	36	3	8.3	29	80.6	11	30.5	..	....	21	58.3				
	No caries	44	17	38.6	6	13.6	1	2.3	..	....	26	59.1				
	Doubtful caries	26	2	7.7	11	42.3	6	23.1	..	....	21	80.0				

* Lactobacilli appeared in pure culture (agar or broth or both) in cultures of 7 subjects with caries (19.4 per cent), in none of those free from caries and in 1 of those with doubtful caries (3.9 per cent). Lactobacilli were accompanied only by yeasts in cultures of 5 (additional) subjects with caries (13.9 per cent) and in none of those who were free from caries or had doubtful caries.

† A streptococcus and a gram-negative bacillus in the same mouth.

‡ A streptococcus.

TABLE 8.—*Concentration of Aciduric Bacteria in the Saliva of Eskimos Correlated with Activity of Dental Caries*

	Condition of Teeth	Estimated Number of Micro-Organisms per Cc. of Saliva: Lactobacilli	Yeasts	Micrococci or Gaffkyae	Staphylococci	Sarcinae	Other Forms
Caries (36 cases)	Range	290-772,630	25-625	25-6,100	175-134,500	50-25,830	.....
	Average of whole group	84,960	70	230	5,230	720	0
	Average of subjects with positive cultures	122,350	230	1,030	37,680	8,660	.....
No caries (44 cases)	Range	80-11,600	.....	5-6,912	2-790	800-407,000	15-25*
	Average of whole group	351	5	239	46	9,270	1
	Average of subjects with positive cultures	2,570	237	955	144	203,900	40
Doubtful caries (26 cases)	Range	262-131,050	20-710	5-6,110	10-1,380	.....	.....
	Average of whole group	10,570	48	737	54	1	62
	Average of subjects with positive cultures	34,290	251	1,743	470	25	1,580

* Fifteen streptococci and 25 gram-negative bacilli were obtained from the same mouth.

the group with doubtful caries occupied the intermediate position. Yeasts were also found to be correlated directly with caries: They appeared in only 1 instance in the cultures of subjects free from caries,

or in 2.3 per cent of the cases, but in 11 instances, or 30.5 per cent of the cases, in the cultures of subjects with active caries. Although not indicated in the table, it is further noteworthy that lactobacilli appeared in pure culture on agar, in broth or in both in cultures of 7 subjects with caries (19.4 per cent), in none of the cultures of subjects free from caries and in the culture of 1 subject with doubtful caries and that lactobacilli were accompanied only by yeasts in cultures of 5 additional subjects with caries, or 13.9 per cent, and in none of the cultures of subjects free from caries or with doubtful caries. In other words, cultures of one third of the subjects with caries yielded lactobacilli, alone or accompanied only by yeasts, whereas the culture of only 1 subject with doubtful caries and no culture of a subject free from caries fell into this category.

The incidence of cocci, conversely, was scattered and appears to lack significance. The cocci of the saliva are, of course, largely inhibited by the low p_H of the mediums used, but since it is reasonable to expect the organisms of dental caries to be capable of withstanding p_H levels of 5 or lower, this fact strengthens the inference that cocci are unimportant in the production of dental caries.

The lactobacillus-caries correlation is supported by the quantitative findings, given in table 8. For each generic type in each clinical group, the table presents the range of concentration, the average computed for the whole group and the average computed for the portion of the group that had positive cultures of the given type. It is evident that lactobacilli appeared in cultures of the group with caries not only more often than in those of the other groups but in distinctly larger numbers, such that the highest single count recorded for the group free from caries, 11,600 organisms per cubic centimeter of saliva, is well below the average for the group with caries, computed to include those with negative plates, 84,960 per cubic centimeter. The values for the group with doubtful caries are again intermediate between those for the other two. The concentration of yeasts did not vary with the activity of caries, although the frequency of their occurrence did, as indicated in table 7. None of the other aciduric types showed a significant quantitative relation to caries. The high average values for staphylococci in cultures of the group with caries depend on only 5 positive cultures and hence may be discounted.

Table 9 shows the geographic distribution of lactobacilli and yeasts, arranged for comparison with table 1. Beyond the data in the table, it was found that lactobacilli were recovered from every geographic point represented by more than 1 subject: in 1 of 14 cases from Quigillingnok, in 1 of 6 from Napakiak, in 1 of 2 from Nunivak Island and in 1 of 4 from Tanunak, Nelson Island. It thus appears that the comparative absence of dental caries in these primitive communities can-

not be attributed to absence of an infective agent in the region. A more refined method of detecting these organisms would doubtlessly show them to be even more widely distributed. Among nonprimitive peoples it seems generally true that dental caries is not the result of infection with these organisms but rather the consequence of some condition which permits their proliferation in a given mouth. Given such a condition, the organisms appear to be readily available in any environment. The occurrence of lactobacilli in mouths of the primitive natives and, indeed, in a few of the mouths free from caries in the present study suggests that among the Eskimos, likewise, the significant causes of dental caries lie elsewhere than in infection.

The data as a whole confirm the qualitative results of Bunting and his collaborators [25] and the quantitative findings of Jay, Hadley, Bunting and Koehne [15e] and likewise support the clinical finding that caries among

TABLE 9.—*Geographic Distribution of Cultures Positive for Lactobacilli and Yeasts* *

Region	Number	Positive Cultures			
		Lactobacilli		Yeasts	
		Number	Percentage	Number	Percentage
Bethel and vicinity	47	28	59.5	13	27.7
Eek	20	8	40.0	3	15.0
Primitive villages	39	7	18.0	1	2.6
Kepnuk	9	3	33.3	0	0

* Compare with table 1.

the Eskimos is similar to caries among other races. The correlation of caries with the presence of yeasts in saliva is in agreement with the early findings of Bunting and Palmerlee,[15a] which have not since had prominent consideration. Although cultures of a majority of the subjects with active caries failed to yield yeasts, the correlation found suggests that these organisms may play a part in the disease, perhaps by symbiotic combination with the lactobacilli.

COMMENT

The data presented in this paper are part of a more comprehensive study of dental caries among a group of Eskimos which includes primitive natives, with little contact with white men, and less primitive natives, in closer association with outside influences. Both the clinical and the bacteriologic findings presented indicate clearly that the rather extensive dental caries which occurs among the less primitive Eskimos is the counterpart of the dental caries found among other peoples, with a single notable difference: The evidence indicates that

25. Bunting and Palmerlee.[15a] Bunting and others.[15 b, c]

dental caries among these Eskimos is largely a disease of recent origin. Its distribution is limited for the most part to the younger natives; the older ones, even though they have lived in or near white settlements for many years, show few indications of the disease. It is perhaps a corollary of this fact that the types of dental caries observed among the natives, which are almost exclusively occlusal and proximal, are those, generally the most common in all populations, which are particularly associated with young persons. If, as scattered evidence and opinion suggest, the varieties of dental caries more commonly associated with adults—particularly caries of smooth surfaces of the teeth in the gingival and root areas—have a somewhat distinctive etiologic basis, the problem of the cause of dental caries among these Eskimos is simplified by the virtual absence of such varieties. The essential identity of the disease among Eskimos with the caries of common experience, moreover, coupled with the relative simplicity of conditions of life among them, to which causative importance may be attached, suggests the value of analysis of those conditions. The results of such an analysis might be applicable to the problem of dental caries not only among the Eskimos but in the young of all peoples. This portion of the investigation is therefore of particular value in that it provides an adequate foundation for the other phases of the study, which are detailed in separate reports.

SUMMARY

A total of 124 Eskimos from Bethel and neighboring settlements, from villages on the lower part of the Kuskokwim River and on the coast of southwestern Alaska, forms the basic material of this study. Clinical data on the incidence and characteristics of dental caries and associated conditions of the mouth among these Eskimos, collected by careful examination with a mouth mirror and explorer, are presented. The results show that dental caries is distinctly more prevalent among natives from settlements in which contact with white men is relatively unrestricted and least prevalent among more primitive groups with a minimum of such contact, confirming the previous findings of other workers among Eskimos as well as other primitive peoples in many parts of the world. The data likewise indicate that the incidence of caries becomes progressively less in groups with advancing average age. This finding, augmented by the more than ordinary predominance among Eskimos of varieties of caries commonly associated with young persons, indicates that the disease among these people is for the most part of recent origin.

Among oral conditions associated with dental caries, deposits of salivary calculus appear with a frequency in inverse ratio to the incidence of dental caries, to an extent only partly accounted for by differences in

age. An apparently similar inverse relation between caries and degree of attrition of the teeth, on the other hand, may depend entirely on the age factor. Irregularities of alinement of the teeth and infrequent hypoplasia of the enamel showed no apparent relation to the distribution of caries.

In accordance with the clinical findings, 106 of the Eskimo subjects were classified for the bacteriologic study into three groups: (*a*) 36 had apparently active dental caries; (*b*) 44 were completely free from caries, and (*c*) 26 could not be placed in either of the preceding groups but were listed as having doubtful caries. Saliva from these 106 Eskimos was plated on tomato agar with a p_H of 5 by the Hadley method and introduced into chopped meat broth mediums which contained 1 per cent of dextrose and had a p_H of 4.7 and of 3.8, respectively. Parallel tests with our agar and with a batch supplied by Dr. Philip Jay, who has used the Hadley method extensively, yielded results in close qualitative and quantitative agreement; the method itself gave satisfactory checks and permitted an adequate differential count of the limited number of generic types in saliva which are capable of growing at a p_H of 5. All types were identified morphologically.

Lactobacilli were found in one or more of the mediums prepared with the saliva of 29 (80.6 per cent) of the subjects with caries, 6 (13.6 per cent) of the subjects free from caries and 11 (42.3 per cent) of the subjects with doubtful caries. The number of lactobacilli per cubic centimeter of saliva averaged 122,350 in the positive plates of subjects with caries, 2,570 in the positive plates of subjects free from caries and 34,290 in the positive plates of subjects with doubtful caries. Yeasts were found in one or more of the mediums in cultures of 11 subjects with caries (30.5 per cent), of 1 subject free from caries (2.3 per cent) and of 6 subjects with doubtful caries (23.1 per cent), in approximately uniform concentration. Lactobacilli appeared either in pure culture or accompanied only by yeasts in cultures of 12 subjects with caries (33.3 per cent), of 1 subject with doubtful caries and of none of the subjects free from caries. Lactobacilli were recovered from at least 1 member of every geographic group studied, including the most primitive as well as the least. No correlation appeared between caries and any of the other organisms—chiefly cocci—that appeared in the cultures.

The bacteriologic data are in agreement with the findings of others who have worked among white subjects and support the clinical observation that the caries which occurs among the Eskimos is similar to that which occurs elsewhere.

Case Reports

CELIAC DISEASE IMITATED BY GIARDIASIS

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Cases of celiac disease have been reported in Central Europe many times, though less frequently than in the English-speaking world. The prognosis of the disease is the same as elsewhere. In a number of the cases death occurs, especially at the age of 2 or 3 years. Many patients have recovered if carefully nursed and if given a carefully planned diet. Restoration of health, that is, of the normal ability to absorb fat from the intestines, takes at least two and usually four to six years. Relaxation of dietetic control may cause quick deterioration, even in patients already relieved from clinical symptoms.

In the following case all the features of celiac disease appeared. The parasitologic examination of the feces revealed infection with Giardia, which suggested a therapy leading to an unusually rapid and effective cure.

REPORT OF A CASE

V. S., a boy, was admitted to the clinic at the age of 25 months, in February 1938. The family history was not significant. The child had one brother, who was 5 years old. The patient weighed 2,750 Gm. at birth; he was breast fed for four months. He developed normally during the first three months of his life; then he had enteritis for a fortnight, passing five or six watery stools every day and losing considerable weight. Diarrhea recurred twice. The child lost 1 to 1.5 Kg. on these occasions, but he weighed 11,500 Gm. at the age of 22 months. From this time on he constantly lost weight, having large pasty foul stools two or three times a day.

Physical examination revealed a pale weak child seriously retarded in development. The weight was 6,850 Gm. and the height 72 cm.; the head measured 47 cm. in circumference, the thorax 47 cm. and the unusually large and protruding abdomen 55 cm. (The average weight at this age is 12,300 Gm., the height 82 cm. and the circumference of the head 48 cm., of the thorax 50 cm. and of the abdomen 45 cm.) Slight signs of rickets were present. The skin was dry, flaccid and atonic and the hair scanty. The muscles were atonic. Examination of the heart and lungs revealed nothing abnormal. The liver was just palpable. Blood tests for syphilis gave negative results, as did intradermal tests for tuberculosis. The hemoglobin content was 62 per cent; the erythrocytes numbered 3,220,000 per cubic millimeter of blood; distinct anisocytosis and poikilocytosis were seen; leukocytes numbered 7,600 per cubic millimeter, and the differential count was normal. No remarkable condition was shown by the urinalysis. Roentgen examination

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of the thorax and of the stomach revealed no abnormality; evacuation was not accelerated or otherwise unusual. Passage and combined double contrast roentgenograms of the bowels revealed a somewhat dilated colon but no pathologic changes; intestinal motility was not increased. Analysis of gastric contents after administration of biscuit and water showed that the value for the total acidity was 8 and the value for the free hydrochloric acid 0, according to the method of Töpfer; the hydrogen ion concentration was 5.5. The sugar content of the blood was 84 mg., the calcium content 7.8 mg. and the phosphorus content 4 mg. per hundred cubic centimeters. Slight osteoporosis was present. The child passed unusually large fetid grayish extremely fatty stools two or three times a day. The feces contained an excessive amount of free fatty acids; the actual p_H was 3.8. Determinations of fermentative acidity revealed perfectly normal conditions; the value for the lipase in the feces was 94 per cent according to the method of Rona and Michaelis.

All the signs and symptoms fitted into the syndrome of celiac disease; all could have been due to an inadequate capacity of absorption. Food substances are well digested in patients with this condition, but the food, especially the fats, cannot be absorbed. The cause of this phenomenon is still unknown. None of the theories has explained the real basis of the disease, and none has been able to show a direct way to recovery.

In the present case, however, the parasitologic examination of the feces revealed a condition which indicated a special direction for therapeusis: Giardia lamblia organisms were numerous in the stools.

Therapy was started with acetarsone at the end of February, 0.1 Gm. being given daily for the first week, and 0.2 and 0.25 Gm. a day during the second and third week, respectively. Then a 0.1 Gm. dose of atabrine (an acridine dye) was given three times a day for five consecutive days. The fat content of the diet was first restricted to 9 Gm. a day; after the third week it was gradually increased to 50 Gm. a day.

The child quickly started to put on weight. He weighed 8,800 Gm. on April 1, when a few parasites were still detectable in the stools, and 9,350 Gm. on April 15, when Giardia could no longer be seen. From this time on the stools were free from parasites. Three weeks later the patient's weight was 10,500 Gm. and six weeks later, at the end of May, 11,750 Gm.; that is, nearly 5 Kg. was gained in three and a half months. At the time of writing, the skin and muscular tone are normal. The abdomen, which no longer protrudes, measures 47 cm. Anemia has disappeared, the hemoglobin content being 78 per cent and the erythrocyte count 4,700,000. The calcium and the phosphorus content of the blood are 10.6 and 5.2 mg., respectively, per hundred cubic centimeters. Stools are passed once a day; they are normal in both quantity and appearance; their p_H is about 6.2. Fecal analyses and other observations to be reported later will explain why the improvement is considered as a sign of recovery.

COMMENT

Absorption of nutritive matter is hindered in every pathologic condition in which the digestive juices do not reach the contents of the intestines. Incomplete absorption in dyspeptic infants has been ascribed to this cause since the time of Biedert. In most cases of celiac disease, however, fermentative activity has been normal. In the present case this was shown, apart from the normal results of determina-

tions of fermentation, by the great amount of split fat in the feces (table 1). Freise and Jahr ascribed the hindrance of absorption in these cases to a primary increase in the speed of peristalsis. The supposition may be true in some cases of celiac disease, but it is not in all. The proportion of excreted nutritive substances may be high with severe diarrhea, but only in those instances in which, owing to the brevity of time or to some other factor, digestion is impaired. If the fermentative processes are efficient, the loss will never exceed 25 or 30 per cent, even with more severe diarrhea than the type associated with celiac disease (two to four stools a day). Moreover, in the present case intestinal motility, as checked by roentgenoscopic examinations, was not accelerated. That the stools are passed several times a day is rather a consequence of the large amounts to be excreted: Water and secretions not being much better absorbed than the foodstuffs, the contents of the intestine are excessively increased.

One must suppose, therefore, that in similar cases some independent disorder affecting the capacity of absorption itself is the basis of the disease. For a long time, however, no such conditions were known. In 1936 the experiments of Laszt and Verzar showed that after extirpation of the adrenal glands absorption of fats is greatly hindered by the lack of the cortical hormone and that metabolism of sugar and salts is severely altered as well. Synthesis of the fatty acids in the villi depends on the cortical hormone. If this is not present, no neutral fat, but only fatty acids, can be found in the mucous membrane of the intestine. A similar deficiency might explain many of the celiac symptoms, but in the present case there were absolutely no signs of Addison's disease to confirm this assumption; moreover, both the red cell picture and the normal value for the blood sugar were against it.

As demonstrated by previous investigations in this clinic, similar hindrance of absorption can be found in some of the children harboring Giardia lamblia. Observation of 155 infected children showed that this parasite may often cause a disease the chronic stage of which is characterized by severely impeded development and by anemia. The circulation of nutritive materials and pigments gave evidence that the capacity of absorption was altered in some of the cases of Giardia infection. The lesion was ameliorated in proportion to the progress of recovery, i. e., to the diminution of the number of parasites. When they disappeared, absorption became normal. The disorder can easily be explained as the result of the mechanical action of Giardia. If present in large numbers the flagellates, adhering by means of their suckers, cover the surface of the intestinal wall. Thus communication between the lumen of the bowels and the rest of the body may partly cease. Digestive juices, flowing in through channels, reach the food without

obstruction. Absorption, on the other hand, since it occurs over an extensive surface, is disturbed. The degree of disturbance is probably in proportion to the area of intestinal surface paralyzed by the adhering layer of parasites. If only a small number of parasites is present, the imperfection of absorption may be too small to be noticeable. On the other hand, there may exist infections severe enough to paralyze extensive surfaces, which may lead, sooner or later, to serious signs of deficiency. Should this occur in children of proper age and perhaps of suitable predisposition, symptoms fitting into the celiac syndrome might arise, as in the present case.

The capacity of absorption can be estimated by comparing the eaten and the excreted amounts of nutritive substances; under certain

TABLE 1.—*Absorption and Excretion of Fat*

	Subject							
	V. S., Child with Celiac Disease						Control Children	
	Before Treatment		During Treatment		After Treatment			
	Feb. 12	Feb. 16	March 2	March 24	April 2	April 12	Healthy	Infected with Giardia
Fat ingested, Gm.	42.3	9.1	9.1	21.6	50.0	50.0	104.0	24.2
Fat excreted, Gm.	32.9	7.3	3.9	5.1	2.8	....	3.1	17.1
Fat excreted, in percentage of ingested fat.	77.9	80.5	42.7	23.4	5.6	....	3.0	70.8
Fat excreted, in percentcentage of dry substance	58.0	20.1	13.7	9.5	7.7	5.0	13.0	46.8
Neutral fat, percentage	20.1	18.0	22.3	16.0	20.8	....	18.0	15.7
Free fatty acids, percentage	72.6	76.6	41.0	34.0	19.0	....	24.0	68.2
Saponified fat, percentage	7.3	5.4	26.7	50.0	60.2	....	58.0	16.1
p_H of feces	3.8	4.2	4.6	4.6	5.8	6.2	6.0	....
Giardia in feces	+	+	+	+	—	—	—	+

conditions it is indicated by the amount of pigment excreted with the urine. Observations concerning the absorption of fats and the excretion of pigment in the present case were as follows:

1. *Absorption of Fat.*—It is known that in a healthy person at least 90 per cent of the introduced fatty substances are absorbed. That means that no more than 8 to 10 per cent of the fat taken in can appear in the feces; generally not even 3 or 4 per cent is present. This usually amounts to about one tenth of the dry substance of the feces. In this patient, however, 80 per cent of the consumed fat reappeared in the feces, and 60 per cent of the dry substance of the feces consisted of fat. Estimations were made according to the method of F. Müller. There was an excessive amount of free fatty acids; the actual reaction of the stools was unusually acid (table 1).

The situation could not be changed by administering a diet low in fats. Of the 9 Gm. of fat given each day, only 20 per cent was

absorbed, 7 Gm. being excreted. The absolute quantity of fat in the feces being less with such a diet, the patients, if judged by the appearance of their stools, show some improvement, although their capacity of absorption invariably remains imperfect.

Treatment gradually changed the pathologic conditions, and perfectly normal data were obtained. After the therapy was ended, only 5.6 per cent of the consumed fat was excreted, and all the values of the patient corresponded to those of a healthy child of the same age used as a control.

The last column of table 1 contains data on a child of the patient's age who was also infected with Giardia lamblia but showed no features of celiac disease. It can be seen that absorption of fat in this child was quite as imperfect as in the patient with celiac disease before treatment. It has previously been mentioned that a similar disturbance

TABLE 2.—*Concentration of Pigments in the Urine* *

	V. S., Child with Celiac Disease	Control Children	
		Healthy	Infected with Giardia
Before treatment	0.095	1.800	0.190
	0.110	1.710	0.080
	0.070	.....	0.100
During treatment: 1st week	0.190		
2d week	0.600		
4th week	1.670		
After treatment	1.580		
	1.790		
	1.750		

* Color values after reduction (F_0) determined according to the method of Heilmeyer.[1]

of absorption had been observed in several other children harboring Giardia.

2. *Excretion of Pigments.*—Estimation of the absorption in the intestines can be made by other means than comparing the eaten and the excreted quantities of nutritive matter. It is known that a great part of the excreted bile from the liver is absorbed in the duodenum and in the jejunum and is again employed in production of bile. If, owing to any cause whatever, the bile is not absorbed in the intestine and is thus excreted with the feces, the body suffers great losses. A part of the absorbed biliary pigments leaves through the kidneys; if the absorptive capacitiy of the intestine is perfect, the concentration of pigments in the urine corresponds to the amount that entered the bowels. The less pigment absorbed from the intestines, the less is excreted with the urine.

The concentration of pigments in the urine normally has a color value after reduction (F_0) of about 1.8, according to the method of

Heilmeyer.[1] For healthy young children it usually varied from 0.9 to 2, while values under 0.9 were never found for children under 3 years of age. The concentration of urinary pigments is increased during the course of many diseases. Therefore it cannot be generally used as a measure of absorption. The values decrease only in such conditions as polyuria. A disease in which the amount of pigments was lessened was not known, no condition having been observed in which the intestinal wall became impermeable. This impermeability is, however, the only possible explanation of the fact that the bile, easily absorbable under normal circumstances, is not taken up by the intestines but is excreted with the feces.

In the present case the values for the concentration of urinary pigment were as shown in table 2. It should be mentioned that no further pathologic change was noticeable either in the quantity or in the composition of the urine.

For the sake of comparison, in table 2 are presented color (F_o) values of 2 control children, those cited in table 1. One of them was healthy and free of parasites, while the other was infected with Giardia lamblia but revealed no symptoms of celiac disease.

SUMMARY

A boy 25 months of age showed the features of celiac disease. He was severely impaired in development, with a large, protruding abdomen, hypotonic muscles, a dry skin, anemia and low calcium and phosphorus values in the blood and osteoporosis. He had large, highly offensive, extremely fatty stools two or three times a day. Examinations revealed serious diminution of the absorptive capacity of the intestines. The condition was attributed to an infection with Giardia lamblia. After expulsion of the parasites the child quickly put on weight; the capacity of the absorption became normal, and the anemia and all the symptoms of celiac disease vanished.

CONCLUSIONS

I by no means suppose or state that in every case celiac disease must be caused by infection with intestinal parasites. The present case, however, makes it appear probable that a primary cause of the celiac syndrome can be detected in some instances and indicates that in case of similar troubles of the intestinal system a parasitologic examination should not be omitted.

1. Heilmeyer, L., and Will, G.: Klinische Farbmessungen: Die spektrophotometrischen Grundlagen der Harnfarbmessung mit dem *Pulfrichschen* Stufenphotometer; Spektrophotometrische Harnfarbanalysen bei Normalen sowie bei Leberschädigung und gesteigerter Hämolyse, Ztschr. f. d. ges. exper. Med. **67**: 111, 1929.

TUMORS OF THE SPINAL CORD IN CHILDREN

REPORT OF A CASE OF TERATOID TUMOR

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The view that neoplasms of the spinal cord in children are rare is not supported by statistics. Forty years ago Schlesinger,[1] in a series of 251 tumors of the spinal cord disclosed at autopsy, found that 24 per cent were in children under 15 years of age. Stookey, in 165 cases in which the diagnosis was verified at the Neurological Institute between 1910 and 1926, found only 8 of the tumors in children under 12. However, it must be added that 2 of the 8 children were operated on before 1922, while in the remaining 6 the condition occurred during the next four years. The apparent increase in frequency is probably explained by the progress made during that period in the recognition of tumors of the spinal cord at this particular clinic. Unfortunately this progress has not obtained generally, as in many cases the lesions are still doubtless overlooked owing to insufficient neurologic information. If the possibility of the occurrence of tumors of the spinal cord in children is repeatedly stressed by neurologists, it is likely that the condition will be recognized in the future in many more cases. It is for this reason and because of the comparative rarity of the pathologic classification of this particular tumor that the following discussion is presented.

The symptoms and signs of a tumor of the spinal cord in a child, as in an adult, depend on the location and size of the growth. Therefore the special diagnostic problems of each case will be present early in the course of the disease.* It is only in the later stages of compression of the spinal cord that complete motor paralysis and a definite sensory level are present. Because the manifestations of a tumor may simulate practically any disease of the cord one should always eliminate the possibility of this condition before accepting a different diagnosis.

Although we shall discuss the symptoms in a certain order, it must not be inferred that they appear in this chronologic sequence.

1. Schlesinger, H.: Beiträge zur Klinik der Rückenmarks- und Wirbeltumoren, Jena, Gustav Fischer, 1898.

Pain may be entirely absent in some cases, while in others it may be the only symptom noted. When the tumor is situated posteriorly, it is likely that the sensory roots will be involved early; pain will be the presenting symptom in this particular instance, and it will radiate over the area of the root or roots involved. It may be of great severity. If the neoplasm is in the cervical region, the muscles of the neck may be held rigid, this protective mechanism suggesting such a diagnosis as meningitis or arthritis of the cervical part of the spine. If the lower dorsal roots are affected, an acute condition of the abdomen requiring operation may be simulated. Indeed, not a few patients with tumor of the cord have been operated on for acute appendicitis or for disease of the gallbladder. When the cauda equina is the site of the lesion there is, sooner or later, sphincteric disturbance, and pain may be referred to the rectum as well as down the legs.

Pains referable to the sensory roots may at first be unilateral, but they invariably become bilateral as the lesion expands. The thought still persists in many minds that there is no lateralization of the pain with tumor of the cord and that this fact eliminates a possible diagnosis of tumor. Reference to the early anatomic-pathologic picture completely dispels this fallacy.

The intensity of the pain is increased when there is a sudden increase in the intraspinal pressure, such as that caused by sneezing, coughing or defecation. This is an important diagnostic point.

Motor weakness may occur early, late or not at all. It varies from clumsiness in the fingers and hands or slight dragging of one foot to complete loss of muscular power. It is usually gradually progressive but may be comparatively sudden in onset. In the latter event one may be misled into thinking that the lesion is inflammatory. When the pyramidal tracts are involved the paralysis obviously will be spastic, while if the lesion is in the cauda equina flaccid paralysis ensues.

Sensory disturbances are subjectively described as numbness, a feeling that the limbs are "asleep," a prickly sensation and so on. Objective sensory loss may not be demonstrable in the early stages. If only one sensory root is irritated it is possible that no loss can be shown objectively on account of the overlapping distribution of nerves to the involved dermatome. A definite sensory level sufficient to warrant a localizing diagnosis occurs late. Vastly better results will be obtained from surgical treatment if the diagnosis can be made when the sensory changes are still subjective. Of a series of 42 cases reported by Spurling, subjective sensory disturbance was noted in 83 per cent. Objective change was demonstrated in 76 per cent.

The reflex changes depend on whether the pyramidal tracts or the conus and the cauda equina are compressed. In the former eventuality one sees exaggerated tendon reflexes below the lesion and diminution or loss of the superficial reflexes. It is a rarity to find the reflexes unchanged, but this can occur.

Studies of the spinal fluid should be made in every instance in which disease of the spinal cord is suspected. Of paramount importance are the mechanics of the fluid, determined by manometric observation on jugular compression and by the chemical composition of the fluid itself. There should be an acute sudden rise in the pressure when the internal jugular veins are compressed, with an equally rapid drop when the pressure is released. In the presence of a complete block in the spinal canal above the point of the puncture, no elevation of the pressure will be seen on the manometer. If the block is only partial, the rise in pressure may be quite as acute as if no block were present, but the descent on release will require a much greater time. There is an indispensable procedure in the diagnostic approach to diseases of the spinal cord.

The most important chemical study is determination of the total protein content of the fluid. In the presence of block the content is increased. Xanthochromia may or may not be present.

In addition to the information obtained at lumbar puncture, the procedure, with the withdrawal of a small amount of fluid, will not infrequently produce an exaggeration of the sensory signs already present. In addition, it may enable one to demonstrate a sensory level that previously could not be ascertained.

Roentgen examination without the injection into the spinal canal of iodized oil or of oxygen offers little. One does not wish to give the impression that a foreign substance should be injected into the subarachnoid space unless it is considered essential for a localizing diagnosis. When the localizing evidence is not definite, however, this procedure is of inestimable value. It should never be done except by one especially trained not only in the actual technic, but in the interpretation of roentgenograms. The oil escapes if operation is done later, but even when it has remained we have never observed any harmful sequelae. In the case to be presented it was through this means alone that the definite upper and lower limits of the tumor could be ascertained.

As for treatment, once the diagnosis is certain surgical removal is the only hope of cure for a tumor of the cord. In view of the fact that a majority of the tumors in this locality are benign, good results are to be expected, provided the patient is referred to the surgeon before the cord is permanently damaged by prolonged pressure. It is amazing to what a degree the cord of a child can recover its normal function after extreme compression.

The following case well illustrates the diagnostic procedures outlined and in addition represents a certain pathologic type that is extremely rare. Teratoid tumors of the cord were adequately reviewed by Hosoi [2] in 1931, at which time only 10 cases had appeared in the literature. In 1934 Bucy and Buchanan reported a case. We have been unable to find additional reports of this type of tumor.

REPORT OF CASE

A 3 year old boy was admitted to St. Vincent's Hospital on April 8, 1937. His birth was normal, and he was not ill until November 1936, six months prior to admission. At this time he complained of pain, first in one leg—the parents were not certain which one—and shortly thereafter in the other. Within two weeks the child was acutely ill with fever; the condition was thought to be meningitis. He was given some spinal injections. After about two weeks he was convalescent, but weakness and trembling of both legs remained. It was then first noticed that the boy dragged or shuffled both feet. This symptom gradually progressed to complete loss of motor power, and for the four months preceding his admission to the hospital the child had not been able to walk. The pain had apparently disappeared after the onset of paralysis.

Neurologic examination revealed a rather undernourished little boy. At the level of the spinous process of the ninth dorsal vertebra there was a dimple, through the minute opening of which protruded two or three strands of hair. No deformity in the vertebral column was apparent. Owing to lack of intelligent cooperation, the results of sensory examination were uncertain, but it could be shown to the examiner's satisfaction that there was no sensation to pinprick below the sixth dorsal segment. There was complete spastic paraplegia. The deep reflexes were markedly exaggerated bilaterally. Bilateral ankle clonus and patellar clonus were observed, and there was a positive Babinski sign on the left. The cremasteric and abdominal reflexes were absent. The impression at that time was that the lesion bore a definite relation to the dimple. Teratoid tumors have not infrequently been accompanied by spina bifida and by pilonidal cysts. However, the febrile attack and the diagnosis of meningitis made by the family physician six months previously could not be ignored. Postmeningitic circumscribed adhesive arachnoiditis could have produced this picture.

It was determined to make a spinal puncture in order to observe the effect of compression of the jugular vein and to study the fluid. The needle was introduced into the fourth lumbar interspace. No fluid was obtained. So certain was the examiner that the canal had actually been entered that 0.5 cc. of iodized poppyseed oil was introduced. When the fluoroscopic table was tilted with the patients' head down, the oil was readily seen to move uniformly until it reached the lower border of the eleventh dorsal vertebra, where it abruptly stopped. With the lower limit of a spinal block thus established, a cisternal puncture was done in order to determine the upper limit. The fluid obtained was crystal clear. Another 0.5 cc. of iodized poppyseed oil was then injected. The opaque material quickly descended to the upper margin of the eighth dorsal vertebra, where a definite filling defect developed along the lower limits of the oil (fig. 1).

2. Hosoi, K.: Intradural Teratoid Tumors of the Spinal Cord: Report of a Case, Arch. Path. **11**:875-883 (June) 1931.

Examination of the spinal fluid showed a negative Wassermann reaction, a cell count of 3 and a total protein content of 10 mg.

Operation was done on the following day, with infiltration of a 0.25 per cent solution of procaine hydrochloride. A linear incision was made from the spinous process of the seventh to that of the twelfth dorsal vertebra, encircling the dimple at the ninth process. The defect proved to be a well demarcated sinus that disappeared into the vertebral canal between the ninth and the tenth spinous process. The laminas of the eighth to the eleventh vertebra were removed. It was then seen that the sinus was an outward fistulous projection of the dura. The dura was opened on the lower aspect of the sinus, and there immediately came into view a cystic tumor. The cord beneath had been compressed to a mere ribbon. The cyst was easily separated from the compressed cord until its upper half was encountered, just at and above the point where the dura was reflected to form the superior portion of the sinus. At this juncture the cyst was ruptured and cheesy sebaceous material escaped. In its entire upper portion the tumor was changed in character, having the appearance of granulation tissue

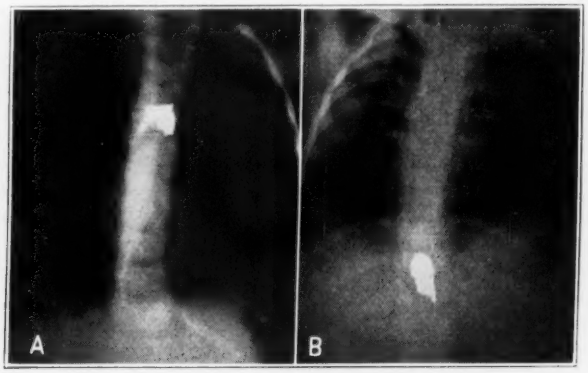

Fig. 1.—Roentgenograms made after injection of iodized poppyseed oil into the spinal canal, *A* showing the upper and *B* the lower limit of a spinal block.

that imperceptibly merged with and invaded the spinal cord, causing its complete destruction at this point throughout its entire diameter. Since it appeared absolutely futile to attain any improvement, the cyst, together with enough of the granulation tissue for biopsy, was excised, and the operative procedure was discontinued. After the sinus was excised, the dura was closed with silk. The muscles, fascia and skin were closed in the usual manner.

At the close of the operation the patient was in a state of profound shock, from which he did not emerge; he died eight hours later.

For pathologic study, sections were made at right angles to the surface of the skin downward through the whole depth of the specimen. Extending deep into the mass from the central dimple on the surface of the skin was a fistula lined by epidermis and containing occasional small nonpigmented hairs. Supporting the epithelium was a sheath of dermis. In it were occasional hair follicles together with sebaceous and coil glands. Erector muscle bundles were frequent. At the lower margin of the specimen was the cup-shaped dome of a cystic cavity lined by epidermis. A residue of cystic contents consisting of old dried epithelial cells and occasional hairs lay on its epithelial surface. The cyst was evidently the dilated lower end of the fistula previously mentioned, but no direct continuity

could be established, since at the levels sectioned all the sections showed an intervening zone containing hair follicles and dermal glands but no epithelial core. The dermal sheath spread out over the top of the cystic cavity; but it, together with the epidermal layer, ended abruptly on one side; on the opposite side it was replaced by simpler fibrous tissue, and the epidermal layer abruptly disappeared, to be replaced by a thick layer of loose granulation tissue (fig. 2). This contained many engorged capillary blood vessels continuous with vessels in the outer wall and was heavily infiltrated by lymphocytes, plasma cells and neutrophils. There were also many phagocytic endothelial leukocytes filled with nuclear débris. Large numbers of leukocytes extended outward into the scar tissue wall, and here numerous eosinophils were added to the other types.

Fig. 2.—Photomicrograph of a longitudinal section through the sinus and the cyst. At the extreme left, but poorly defined, is the lower end of the skin-lined lumen which extended downward from the surface. At the right is the dome of the skin-lined cyst that lay on the cord. Between and about them the distorted dermis contains sebaceous and coil glands, smooth muscle bundles and occasional hair follicles. The cyst contains desquamated epithelium, hairs and débris.

Since the wall had been broken it was difficult to make out exact relationships at the bottom of the cyst, but it appeared that here there was a closely applied if not continuous layer of different structure, which probably represented the spinal meninges, in close juxtaposition to the outer surface of the cyst. This tissue layer was a feltlike mass of collagenous bundles with relatively few nuclei. There was an occasional suggestion of a covering meningothelial layer, and frequent, relatively large blood vessels lay in the superficial zone, some of them of sinusoidal type. Extending through this tissue were noted occasional bundles of medullated nerve fibers.

SUMMARY

The incidence, symptomatology and physical findings of tumors of the spinal cord in children are discussed.

The importance of thorough neurologic study, including the mechanics and chemistry of the spinal fluid and, when indicated, the injection of opaque material in cases of suspected spinal cord disease is emphasized.

The pathologic report in this case revealed a teratoid tumor of the cord; this type of tumor is extremely rare, only 11 previous cases having been found in the literature.

SPONTANEOUS PNEUMOTHORAX IN THE NEWBORN

REPORT OF A CASE IN WHICH THE MECHANISM WAS DEMONSTRATED

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The case of spontaneous pneumothorax reported here is presented not only because of the rarity of the condition but because it is the only instance that I have been able to find in which roentgen evidence of the mechanism has been available.

When one reviews the literature it soon becomes evident that there is a tremendous amount of confusion as to the limitations that should be applied to the descriptive term spontaneous pneumothorax in the newborn. It would seem that the term could be better applied if it were not extended so as to include the entire neonatal period, ordinarily reckoned at about one month, but were limited to the period between birth and the establishment of the normal vital processes. This period then would be limited to the first four or five days of life, and lesions that made their first appearance after this time might better be considered as disturbances having a separate cause.

The reason for this differentiation is that there is a group of symptom complexes that arise at the onset of respiration and are characteristically different from disturbances arising at a later date. In this group are congenital deformity, congenital atelectasis and mechanical interference with respiration.

The group which consists of the cases of congenital malformation of the respiratory tract, of course, requires separate treatment. Atelectasis may be due either to mechanical interference with respiration or to intrinsic factors which prevent proper aeration of the lung. Mechanical interference with respiration may give rise either to atelectasis or, occasionally, to emphysema, followed by rupture of the lung and pneumothorax. The term spontaneous also has particular significance in this group because the lesion, as it occurs, is a part of the primary mechanism and is not due to the intervention of any other factor, particularly the factor of infection.

From the Beth Israel Hospital.

In 1928 Scott,[1] in an exhaustive study of the literature on spontaneous pneumothorax in children, reported a survey of 177 cases. His description included all cases of pneumothorax in which the cause was not traumatic. In 51 of these cases, or in 28.82 per cent, the condition was of tuberculous origin. In the others the cause varied from abscess of the lung due to a foreign body to chronic bronchitis and typhoid. Only 4 cases of pneumothorax in newborn children were reported.

It becomes immediately evident from a study of these 4 cases that the onset of the pneumothorax is determined by a special factor which bears no relation to the pneumothorax that occurs after the tissue of the lung has been destroyed by infection or traumatization. Therefore it would seem that these 4 cases should be made the basis of an etiologic classification in which pneumothorax is the result of the efforts of the child to establish its respiration.

The histories of all these cases are similar. The child immediately after birth either breathes normally or has only slight difficulty in respiration. The amount of cyanosis and dyspnea is not more than is commonly observed in newborn children. The progress during the first two or three days is marked by only slightly increasing respiratory embarrassment. An examination of the chest at this time would probably result in the diagnosis of partial atelectasis, on account of the absence of breath sounds in a large portion of the lung. Careful percussion might possibly reveal hyperresonance, but this finding was not mentioned in the reports and was not demonstrable in my case.

At any time from the third to the fifth or sixth day the child suddenly goes into shock; respiratory and circulatory embarrassment are severe, and within a few days the child dies. A roentgenogram taken at this time reveals a completely or almost completely collapsed lung, with total pneumothorax of the affected side, which causes marked shifting of the heart and great vessels. If aspiration is done, air is released, usually under tension.

This characteristic picture I am now able to report in 5 cases from the literature and in 1 case of my own. Although from the time of the first description, that of Ruge,[2] it was felt that the lesion was caused by a ball valve type of obstruction in a primary bronchus, due either to mucus or to meconium, and that emphysema probably preceded the pneumothorax, no one previously has been able to demonstrate the stage of emphysema. In all the reported cases the first roentgenogram was taken after the rupture of the lung had occurred and the patient

1. Scott, A. J.: Spontaneous Pneumothorax in Children: Statistical Study of Literature, with Case Reports, Tr. Sect. Dis. Child., A. M. A., 1928, p. 59.

2. Ruge, C.: Pneumothorax bei einem Neugebornen, Ztschr. f. Geburtsh. u. Gynäk. **2**:31. 1878.

already had pneumothorax. In none of these cases was the primary source of the involvement apparent at autopsy. In no instance was a congenital anomaly of a primary bronchus demonstrated, and only rarely was it possible to demonstrate the point of rupture of the lung.

The reason that it has not been possible to demonstrate the primary cause of the obstruction is that with the relaxation of death a movable obstruction of the type necessary to act mechanically as a ball valve naturally will flow freely out of the tissues. The lack of ability to demonstrate the point of rupture in the lung is not at first glance to be so easily explained.

Hotz,[3] however, has shown experimentally that when rupture of the lung occurs under conditions similar to those existing in these cases, that is, when constantly increasing intra-alveolar tension results in spreading of the pulmonary tissue and final rupture, the rupture occurs near the free knifelike margin of the lung. This was readily overlooked on the autopsy table, unless special methods of staining were used. Ordinarily, even under experimental conditions, the point of rupture could not be demonstrated.

In addition to this massive pneumothorax, there frequently occurs in newborn children a variety of partial pneumothorax, the so-called mantle type. In these cases, owing to the strenuous attempts at respiration that the infant makes, there may be ruptures of small emphysematous blebs. A small amount of air from these blebs escapes into the pleural cavity and, rising to the apex of the lung, gives the mantle phenomenon. This type of pneumothorax is of no great significance and disappears spontaneously.

REPORT OF CASES

In 1878 Ruge[2] reported the occurrence of pneumothorax in a newborn boy.

CASE 1.—Birth occurred by breech presentation; the infant was delivered feet first, but delivery of the arms and head was not difficult. He was moderately asphyxiated when born but cried considerably during the night. The following morning he suddenly became cyanotic, and death occurred shortly afterward.

When the left half of the thorax was opened at autopsy, air rushed out. The heart was displaced to the right, as was the left lobe of the thymus. The left lung was pressed against the spinal column. When placed in water, it sank and showed some small areas containing air. There was a small emphysematous area, and the pleura showed an irregular tear about 3 cm. long. There was some free blood in the pleural cavity. The right lung was normal.

Flipse[4] in 1928 also reported the occurrence of pneumothorax in a newborn infant.

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3. Hotz, A.: Ueber partiellen Spontanpneumothorax beim Neugeborenen, Schweiz. med. Wchnschr. **64**:209, 1934.

4. Flipse, M. J.: Pneumothorax in Newborn Infant: Case Report, J. Florida M. A. **14**:403, 1928.

CASE 2.—The child was delivered by forceps. When he attempted to breathe, little air entered the lungs. It was necessary to introduce a small tracheal catheter. Respiration was established in a few moments but was of an unusual type. Expansion of the chest was limited almost entirely to the left side. The catheter was withdrawn, and the child cried in a feeble but normal manner. Cyanosis, however, developed on slight exertion.

Roentgen study showed the heart to be displaced almost completely to the right of the sternum. The left lung appeared about 50 per cent collapsed, and a well defined area of pneumothorax surrounded it. By the use of oxygen during cyanosis the child was kept alive. Roentgenograms made at intervals of twenty-four hours showed progressive collapse of the left lung until the infant was 2 days old, when there was total collapse.

Thirty cubic centimeters of air was removed from the left side of the thorax by puncture in the midaxillary region. Immediate roentgen examination showed that the heart was nearer the normal position and that there was some expansion of the left lung.

On the following day the lung was again collapsed, and 18 cc. of air was withdrawn. Shortly afterward stridor, retraction of the thorax and cyanosis developed. Oxygen was administered. Roentgenograms taken on the following day showed the left lung to be in apposition with the wall of the chest except along the lower border. The heart was in practically normal position, and the general condition of the child was satisfactory.

In addition to these 2 cases, reviewed by Stein, Donahoe [5] in 1932 reported 2 cases:

CASE 3.—A girl was delivered by podalic version and breech extraction. The baby cried lustily at birth and required no resuscitation, nor did she show any signs of respiratory embarrassment. She seemed perfectly normal in every way; but by the end of the second day the nurse was not satisfied that the baby was swallowing as it should, and the child was seen by the physician for that reason.

The infant was well developed, weighed 8 pounds (3,629 Gm.) and was normal in every way, except for the findings in the chest. Respiration was free, easy and regular but of the abdominal type. Failure of the right side of the chest to participate in the respiratory excursion was plainly evident. The breath sounds were distant on the right though audible throughout. On roentgen examination at this time, at the age of 2 days, the child showed complete pneumothorax of the right side. No treatment was instituted, and the child apparently did well, with gradual reestablishment of the respiration and reinflation of the lung. By the end of a week there was no doubt that the right side of the chest was becoming more normal. It was participating a little in the respiratory excursion with less abdominal effort and less retraction of the costal margin, and percussion and auscultation were not so different on the two sides. Three weeks after birth roentgen examination showed normal expiration of the lung and no air in the pleural space.

CASE 4.—A boy born by spontaneous delivery showed respiratory difficulty from birth and also had sclerema neonatorum. On the fifth day, while nursing, the child had a sudden choking spell and became cyanotic and dyspneic. A roentgenogram taken at this time showed pneumothorax on the right, fully one half of the right lung being collapsed.

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5. Donahoe, W. E.: Pneumothorax in a Newborn Infant, Journal-Lancet **52**: 699, 1932.

Storts and James [6] reported the following case:

CASE 5.—A baby was delivered by episiotomy and low forceps, labor having been induced with castor oil and quinine. Asphyxia pallida was present at birth. After aspiration of mucus, gentle mouth to mouth breathing was started. The baby soon breathed regularly and had a fairly normal cry. The infant did well until the second day, when there was some difficulty in swallowing. On the third day the baby nursed better, but on the night of the third day cyanosis and extreme restlessness developed. No breath sounds could be heard over the left side of the chest, and there was no dulness to percussion.

Roentgen study of the chest revealed pneumothorax. With the administration of oxygen the lung reexpanded, so that by the end of four weeks roentgen examination showed that the condition of the chest had returned to normal.

Storts and Janes stated the belief that the cause might have been trauma due to the mouth to mouth respiration in addition to congenital structural weakness of the left lung.

The report of my case follows:

CASE 6.—Mrs. G. M., aged 34, had had six children. All previous deliveries were normal. Four children were alive and well. One child died shortly after birth, from prematurity. The family history contained no other important facts. The woman was admitted to the hospital in labor. The infant was in the left occipitoanterior position; after an active labor lasting about four hours an apparently normal boy was delivered. The weight at birth was 5 pounds and 7½ ounces (2,481 Gm.). No anomalies were observed. The baby cried readily and had no cyanosis. About four hours after birth the infant began to show intermittent cyanotic spells.

The following day the condition seemed somewhat better, but late that afternoon cyanosis became much more marked. The child was seen by the physician at this time. He was 2 days old, well formed and moderately cyanotic. On examination, no respiratory sounds were heard over the whole of the right lung. It was noted that there was little respiratory movement of the right side of the chest. On percussion there seemed to be some slight loss of resonance.

The diagnosis was atelectasis of a portion of the right lung; oxygen was given at this time. Roentgen examination showed emphysema of the entire right pulmonic zone. This was thought to be responsible for the increase of the intercostal spaces on this side. The condition suggested the likelihood of a ball valve occlusion of the larger bronchi, this occlusion permitting ingress but not egress of the air. The ventilation and aeration of the left side were fairly good. The roentgen diagnosis was emphysema on the right, probably due to ball valve occlusion. In the figure *A* shows the roentgenogram made at this time.

With the information obtained from the roentgenogram and from the report, a bronchoscopic study was made. The larynx was exposed, a direct bronchoscope was inserted into the right bronchus, and some secretion was sucked out. There was little change in the condition of the child. The following day he suddenly went into shock; there were increased dyspnea and marked cyanosis. Roentgen examination made at this time, when the boy was 3 days old, showed pneumothorax extending up the lateral peripheral wall, mainly observed at the upper half of

6. Storts, B. P., and James, H. C.: Pneumothorax in a Newborn, Arch. Pediat. **53**:744, 1936.

the thorax. This resulted in compression of the pulmonary structure and displacement of the heart to the opposite side. There was an extremely slight degree of ventilation and of aeration of the lower lobe of the right lung. The final diagnosis was pneumothorax with collapse of the lung. No treatment was instituted, aside from the administration of oxygen, and on the following day the child died. In the figure *B* shows the roentgenogram made at this time.

Postmortem Examination.—The body measured 19 inches (48 cm.) in length and weighed 2,240 Gm. There was no external evidence of injury.

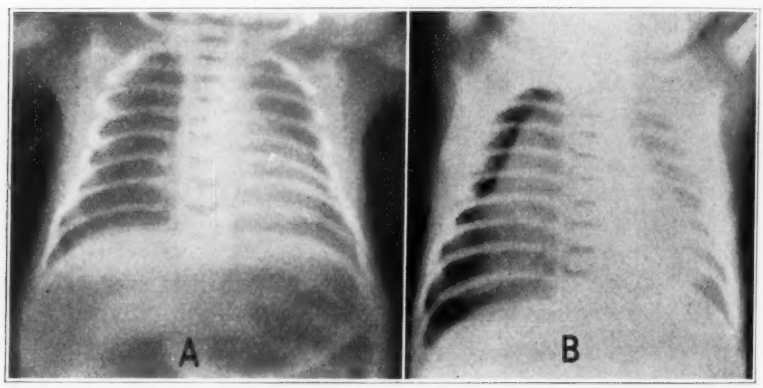
There was no free fluid in the peritoneal cavity. The umbilical vein was patent.

The pleural cavities contained no free fluid.

The pericardial sac contained a small amount of clear amber fluid.

The thymus was small. Cut sections showed a sparse amount of glandular tissue.

The thoracic organs were removed en masse.



A (case 6), roentgenogram showing emphysema. Note the hyperaeration. Air enters the lung but is blocked in exit. *B* shows spontaneous pneumothorax resulting in compression collapse with rupture of the lung.

The heart appeared of normal size and consistency. It was saved for pyroxylin sections.

The trachea was clear. There was no evidence of obstruction at the bifurcation of the bronchi. Each bronchus with its bifurcations was opened until mechanical difficulties ensued. There was no evidence of obstruction.

The left lung superficially showed small areas of emphysema. Cut section showed a moist, light red surface with no gross evidence of any pneumonic process. The right lung showed no evidence of emphysema. Cut section showed an appearance somewhat similar to that of the left lung. The lower lobe appeared somewhat darker and slightly atelectatic. No gross signs of pneumonia could be made out.

The spleen was of normal size and consistency; it weighed 12 Gm. Cut section showed a moist, deep red surface. The malpighian corpuscles were indistinct.

The stomach contained a moderate amount of greenish yellow mucoid fluid. The pylorus appeared normal. Pressure over the gallbladder produced brownish bile through the papilla of Vatêr. The rest of the intestine appeared normal.

The pancreas was of normal size and was moderately firm. Cut section showed a well packed glandular parenchyma.

The liver was of normal size; it weighed 105 Gm. The capsule was smooth and glistening. Cut section showed a rather homogeneous, dull, reddish brown surface. Hepatic lobulation could not be distinguished.

The left adrenal gland was of normal size and consistency. Cut section showed a slightly swollen cortex with little medulla. The right adrenal gland was similar.

The left kidney weighed 20 Gm. Cut section showed a lobulated surface with normal relation of the cortex to the medulla. The capsule stripped easily, leaving a smooth and glistening surface. The right kidney weighed 17 Gm. It was otherwise similar to the left. The bladder was somewhat distended, containing about 20 cc. of clear, golden yellow urine.

On reflecting the scalp a small hematoma was seen over the right parietal region. The brain was somewhat edematous. There was no evidence of any intracranial hemorrhage. The falx cerebri and the tentoria were intact. The ventricles showed no evidence of hemorrhage and were of essentially normal size.

Diagnosis.—The cause of death was an obstruction to the bronchus of the right lung, removed at bronchoscopic examination.

The secondary or terminal lesion was spontaneous pneumothorax (figs. 1 and 2).

Jacob Stein, in reporting 4 cases of spontaneous pneumothorax and adding 1 of his own, also included in this group the following cases:

CASE 1.—In 1917 Scheltema[7] reported the occurrence of pneumothorax in a child of 7 weeks, with symptoms noted from birth. After normal labor the baby was born asphyxiated. The mother said that in breathing the child moved its sides, suggesting exaggerated inspiratory retraction. This sign was found to be bilateral and appeared only in the lowermost portion of the thorax, more on the left than on the right. Respiration was somewhat accelerated, but the child presented a normal, well nourished appearance. When the infant cried, slight cyanosis appeared.

On percussion, a somewhat muffled sound with a tympanitic note was heard in front and behind on the left. On the right, anteriorly, distinct dulness began below the clavicle; it was bounded externally by the nipple on the right and by the sternum on the left. The apex beat could not be felt at the usual site. As a weak apex beat could be felt on the right and cardiac dulness was not present on the left, the heart was presumably displaced to the right. On the right the usual puerile breathing was heard; on the left, weakened breathing, and in the flank, practically no breathing.

The symptoms pointed to the absence of the lung in the left half of the thorax and to considerable displacement of the heart with mediastinum to the right. This assumption was confirmed by the roentgen observations and by transillumination at that time and three months later.

CASE 2.—Smith,[8] in 1919 reported the occurrence of pneumothorax in an infant first examined at the age of 7 weeks. The labor was normal, and the child breathed after brief resuscitation. The infant had always breathed rapidly and with difficulty. It was brought to the hospital because of eczema on the face and buttocks.

7. Scheltema: Left Sided Pneumothorax Present at Birth, Nederl. maandschr. v. verlosk. **6**:407, 1917.

8. Smith, C. H.: Complete Pneumothorax, Arch. Pediat. **36**:184, 1919.

The lungs showed hyperresonance on the left, with absence of breath sounds. The heart was displaced to the right, and the breath sounds in the upper part of the right lung were poor. Roentgen examination showed cloudiness in this portion of the lung. Rales were present in both lungs.

When the child was 3 months of age, the condition became worse. The infant had several convulsions, and aspiration of the chest drew air. The right lung became filled with rales; bronchopneumonia developed, and the child died. Pneumonia was not present before the onset of the trouble. The diagnosis was complete pneumothorax on the left with subcutaneous emphysema of the left side of the chest.

The report of Stein's [9] own case follows:

CASE 3.—K., a boy, was first seen by the physician, at the age of 1 week, because of vomiting and inability to gain weight. The mother was normal; the patient was her first child, and the delivery had been instrumental. So far as the history showed, there was no cyanosis or dyspnea at birth.

Physical examination at the age of 1 week gave negative findings except for the observations on the chest. Respiratory symptoms and cyanosis were absent. There was tympany over the entire right side of the chest, and voice and breath sounds were absent on this side. The heart was displaced to the left, the right border being at the midsternal line.

Fluoroscopic examination showed the entire right side of the chest to be filled with air, the heart pushed over to the left and what appeared to be the right lung situated at the root.

A barium sulfate meal was given to rule out diaphragmatic hernia and eventration. It showed the stomach to be below the diaphragm on the left and corroborated the previous observations.

When the case was reported the child was 2 years old; he was physically small for his age and showed the characteristic pigeon-like deformity of the chest. He had had several attacks of bronchitis in the left lung without undue consequences. At no time had he suffered from attacks of cyanosis or dyspnea. Fluoroscopic examination had been performed many times during his two years of life, with no change in the picture. At no time had there been any apparent absorption of the air.

Possible etiologic factors had not become evident. The tuberculin reaction had been negative with as much as 5 mg. of tuberculin. A bronchial fistula, however, could not be eliminated as contributing to the phenomenon. There had never been any evidence of infection.

The evidence at hand would seem to make it inadvisable to include the last 3 cases in the same classification as the 6 cases first reported. The case reported by Scheltema is commented on by Stein as follows:

The most plausible explanation for the condition would seem to be aplasia of the lung with an open communication between the pleuraless thoracic cavity and the bronchus. Diaphragmatic hernia could be excluded. The reason for the absence of fluid was not clear, but the condition could be clinically defined as pneumothorax.

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9. Stein, J.: Congenital Pneumothorax: Review of the Literature and Report of a Case, Am. J. Dis. Child. **40**:89 (July) 1930.

From the evidence in the record, this seems to be a fair evaluation of the condition. In the case reported by Smith, the history seems to point to infection of the lung with subsequent rupture and the formation of pyopneumothorax and with terminal pneumonia.

In Stein's own case, on further investigation the lesion proved to be a cyst of the lung.[10]

SUMMARY AND CONCLUSIONS

I have reviewed the literature and am able to report 5 cases of a condition that should be classified as spontaneous pneumothorax in the newborn; to these I have added 1 case of my own. I believe that the term spontaneous pneumothorax in the newborn should be restricted to cases in which a ball valve type of obstruction occurring at the onset of respiration causes emphysema which is followed by rupture of the lung and pneumothorax.

I am able to present, for the first time, roentgen evidence of the occurrence of both of these stages. In the figure, *A*, which shows the presence of acute emphysema in a newborn child, is, I believe, unique. Although it has long been held that the rupture of the lung in spontaneous pneumothorax of the newborn follows a ball valve type of obstruction and emphysema, I believe that this is the first time that actual roentgen evidence to support this contention has been obtained.

10. Stein, C. H., cited by Glaser, J., and Landau, D. B.: Pneumothorax of Newborn, Am. J. Dis. Child. **50**:986 (Oct.) 1935.

Progress in Pediatrics

PUBLIC RESPONSIBILITY FOR SAFEGUARDING THE HEALTH OF CHILDREN

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In view of the present nationwide interest in developing and expanding public health work and maternal and child health services to include medical care of the sick, it seems timely to discuss public responsibility for safeguarding the health of children, to trace the growth of this responsibility in the nation and its reflection in political action, to report progress in public administration and to point out gaps in the present child health program. Public concern for the health and welfare of children is a relatively recent development, dependent in large measure on the evolution during the past century of basic knowledge of causes of disease, of methods of prevention and treatment, of the processes of growth and development and of the effect of social and economic factors on the child's physical and emotional well-being. Public action in the form of protective legislation or legislation to provide for health and welfare services has come gradually and unevenly in the states. Only in the past twenty-five years has federal legislation been enacted to protect children from exploitation in industry or to aid in raising to optimum standards the level of opportunity for health and welfare among children of all states.

Though this discussion will deal largely with the development of public responsibility and public action, recognition must be given at the outset to the many brilliant contributions to knowledge of the care of children made through research and through the clinical observations of physicians devoting themselves to the care of sick children. The great volume of service that has been rendered to children and to the development of the whole program of child welfare by voluntary organizations and agencies and by individual citizens is equally notable. History demonstrates it at every stage. Individual initiative and voluntary undertakings by nongovernmental groups of citizens, both pro-

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fessional and lay, will undoubtedly continue to make important contributions to the body of facts on which future programs will be built and to the standards of administrative practice. But woven through the history of child welfare is a thread of political action, at first slender and weak but becoming stronger as the decades and centuries pass, until today there has emerged a pattern of public action which if filled out in all its parts and kept flexible in application should ultimately achieve results for children that a great democracy can look on with satisfaction.

What are some of the events of the past three centuries which have helped design the pattern of the present program of child care? Even at the beginning of this country's history, three centuries ago, and during the succeeding two centuries, when in Europe the public conscience regarding child care was dullest and an infant's life was apparently valued at naught, the colonists had certain rather vague conceptions of the rights of mothers and children to health and protection. Records are meager, but they give evidence of some sense of public responsibilty for the care of mothers and infants and the welfare of older children. The need for education, on the other hand, was with good reason more apparent than was the need for social protection or supervision of the health of children. Society was relatively simple, and children were allowed little social freedom; few basic facts related to the control or treatment of communicable disease, the feeding of children and the control of the milk and the water supply were available to guide physicians and public servants in the conservation of child life. To build a democracy an intelligent citizenry was necessary, and so free education early became a basic public policy. To build a strong and healthy child population, able to use the advantages of education, required knowledge of causes of morbidity and mortality, of the incidence of disease and of methods of its prevention and control which had not yet been acquired. And so the development of a major public program for the conservation of child life lagged approximately a century behind the development of public education, awaiting the scientific progress that would make it possible in the late nineteenth and the twentieth century.

In 1587 was born on Roanoke Island, off the coast of North Carolina, Virginia Dare, the first child of English parents to be born in North America. In 1620, on the Mayflower, as she rode at anchor in Cape Cod Bay, was born Peregrine White, the first child of English parents to be born in New England. It is not known who attended the birth of Virginia Dare, as all records of that ill fated colony are lost. The birth of Peregrine White, however, was without much doubt attended by Mrs. Samuel Fuller, the wife of the deacon of the church and surgeon of the settlement. The records show that she was an experi-

enced midwife but do not indicate whether she was paid for her services by the community. The services of her deacon-surgeon husband, however, were freely available to all in the settlement, and no attempt was made to collect payment from individual patients. Fourteen years later Anne Hutchinson, more famous for her religious activities than for her midwifery, collected individual fees from the members of the Massachusetts Bay colony.

It was the custom of the London company that sponsored the colonies in Virginia as a commercial venture to provide surgeons or physicians, to pay salaries for their services, to provide drugs and equipment and to instruct them to care for the needs of the people without cost to individuals. The company formulated rules and regulations pertaining to health which reflected the best thought of the time and in 1612 went so far as to establish an eighty bed hospital near Jamestown. But this interest of the London company in health did not extend to obstetrics, a circumstance that merely reflected the attitude of the medical men of the day in England. Midwives went to Virginia on their own initiative and worked on a private fee basis; they were not a part of the London company's provision for medical care. Since midwives of that day in England received their training through experience only, the skill of the Virginia midwives was probably not great.

The records of the Dutch West India Company show that from 1629, when the charter was granted to the patroons and colonists, the need for medical care was recognized. At this time in Holland physicians were already showing interest in the art of obstetrics and in providing midwives with education for their profession. This attitude of the Dutch physicians was reflected in the colonies, for the midwives in the Manhattan colony were reported as having had some training. Among the first in New Amsterdam (1638) was Lisbert Ducken, for whom the colony built a house. The second midwife on record was Tryntje Jones, who was midwife to the colony in 1644 and was paid by the council of the colony for obstetric work among the poor. This is one of the earliest recorded instances of the assumption by a local government of responsibility for maternity care.

The milestones that mark progress in public responsibility for the health of children during the seventeenth and eighteenth centuries are relatively few. Conditions under which children lived in the towns and villages were good compared with the evil conditions of the large cities of England. It must be remembered that in this country even at the time of the American Revolution there were only seven towns with more than 5,000 inhabitants. Though smallpox was one of the commonest and most fatal diseases of childhood, scarlet fever, diphtheria, measles and whooping cough also took their toll of children's lives freely.

The earliest quarantine laws, passed about 1650, dealt primarily with smallpox; they attempted to protect the colonies against infection from without by prohibiting the docking of "sickly ships." About 1700 Massachusetts passed an ordinance requiring that persons suffering from smallpox remain in certain designated houses, from which the healthy members of the community were warned away by a red flag. However, lack of knowledge of the causes and methods of transmission of disease combined with inadequate enforcement of the existing regulations made these early public health measures ineffective in preventing the spread of the infection.

A great step forward in the control of smallpox came when in 1721 Cotton Mather introduced into this country the procedure of inoculation with virus from a human subject. The method proved to be effective in reducing both morbidity and mortality. Many progressive persons arranged for inoculation of themselves and their children, and "inoculating hospitals" sprang up to serve them in many localities. Legislation was passed in a number of the colonies, not requiring inoculation as a preventive procedure but controlling the places where inoculation might be undertaken so as to protect the other inhabitants of the towns. In 1777, by military order of General Washington, the troops at Valley Forge were inoculated against smallpox.

Major reductions in the incidence of smallpox, especially among children, did not come until after 1800, when in Boston Dr. Benjamin Waterhouse, following instructions from Jenner, introduced vaccination by vaccinating his own five children and thereafter permitting his 12 year old son to be publicly inoculated with matter from a patient suffering from smallpox. The effectiveness and simplicity of vaccination quickly insured its popularity. President Jefferson lent Waterhouse much support in his campaign to make vaccination a universal protection, and his interest is reflected in his order to his secretary, Captain Merriweather Lewis, to vaccinate all members of the Lewis and Clark expedition. In 1809 two towns in Massachusetts offered free vaccination, and in the same year an act was passed in Massachusetts requiring all towns to provide for vaccination of their inhabitants. It was not until 1855, however, that the first state law to make vaccination compulsory was passed, also in Massachusetts.

During the seventeenth and eighteenth centuries infant mortality was high, but records were poor because "bills of mortality" were not required to be kept in the towns to any considerable extent until after the beginning of the nineteenth century. The middle of the seventeenth century had witnessed the awakening of medicine in Europe and in England, and physicians were beginning to take an interest in the diseases of children. Among other diseases, rickets and scurvy, smallpox, measles and diphtheria (described as angina) were recognized as

disease entities, and diarrheal diseases were prevalent; but treatment included only the usual procedures of bloodletting and purging and the use of "simples." Many physicians in their treatises on medicine described diseases and conditions found in infants and children, but even well into the eighteenth century many preferred to leave the care of the infant to the midwives and women because the physicians were "at a loss to know what to order for it." There were no physicians who specialized in the care of children. The art of obstetrics, also, was still in its infancy and largely practiced by midwives. In 1741 the first foundling hospital for newborn infants was established in London, a century after the first institution of that kind had been established by St. Vincent de Paul in Paris. In 1769 the first free dispensary for children was opened in London.

In the American colonies physicians were fewer and knowledge no greater than in Europe; but the public conscience was perhaps a bit stronger, and living conditions in the small towns and villages were somewhat less conducive to the spread of disease. It was not until after the colonial period, from about 1790 to 1800, that the problem of "summer diarrhea" assumed any importance in medical literature, a fact that can probably be accounted for by the growth of towns and cities at this time and the development of common supplies of milk and food. The infant mortality of the nineteenth century was tremendously high, as is shown by the vital statistics of individual towns and cities. The first federal census was taken in 1790, but the data collected then and throughout the nineteenth century were useless in a study of infant mortality, since they merely included counts of persons living in the various states and other information not pertinent to mortality statistics.

In 1846 Lemuel Shattuck, in his report of the "Census of Boston for the year 1845," statistically analyzed records of deaths in the first year of life for the years 1811 to 1845 and made certain comparisons of Boston with other cities. By so doing he presented data that have formed the basis of statistical studies of infant mortality ever since. Among other pertinent facts he pointed out "that the number of births which take place in a given time in a population, and the number and ages of the living, as well as the ages at death, are indispensable elements of information for correct estimates and comparisons of this kind."

That Lemuel Shattuck was far ahead of his time in this respect, as in many others, is manifested in the "Report of the Sanitary Commission of Massachusetts" published in 1850. This report, signed by Shattuck as the first of three commissioners, recommended the establishment of a state board of health; though the time was not yet ripe for the major advances in the child health program, it pointed out that

attention should be given to the problems of the care of children as part of a public health program. The report states:

> From one-third to one-half of all the deaths in the populous cities and villages, and about one-quarter in all places, are those of children under five years of age. . . . This is a great, an all-important matter, and deserves to be thoroughly examined and carefully studied in all its bearings by fathers and mothers, and those who expect to be fathers and mothers, as well as by nurses, governesses, teachers, and all others interested in the care of the young. The subject is too great, however, for discussion in this connection. Our purpose is merely to call public attention to it, as one of the sanitary measures in which there is great room for reform, and in which real reform would be immensely beneficial.

In 1843, three years before Shattuck's report was published, Horace Mann, in his sixth report as secretary of the Massachusetts Board of Education, had made a strong plea for instruction in health and hygiene through the common school curriculum, outlining in great detail the content of such a course. This was the period when public schools were being permanently established by legislative act in many of the states. The same period was seeing the beginnings of the public health movement.

During the half century that was closing in 1850 the nation had been faced with numerous problems arising from its rapid industrial development, increasing immigration from Europe and steady expansion into the West. Child labor was already an evil that the states were being forced to recognize. Infant mortality and maternal mortality were still high and were accepted with a fatalistic attitude. Just before the turn of the half century an event occurred that should have radically changed the trend of the maternal death rate but did not, partly because the bacterial origin of disease was not yet known and partly because the public was not yet sufficiently educated to understand and accept preventive measures. I refer, of course, to the presentation by Oliver Wendell Holmes, in 1843, of his lecture, "The Contagiousness of Puerperal Fever."

The observations presented by Dr. Holmes were forerunners of a long series of scientific discoveries, made in the last half of the nineteenth century and the first quarter of the twentieth century, which were to revolutionize public health and medical care and pave the way for a rapid development of the maternal and child health program as it is known today. The discovery of the bacterial origin of certain diseases and the parasitic origin of others, the use of pasteurization to destroy bacteria in milk, the use of serum as a therapeutic agent, the preparation of immunizing substances, the newer knowledge of the elements of nutrition, including the discovery of vitamins and their relation to deficiency diseases, the development and greater use of physical and chemical

therapeutic agents and of the psychobiologic understanding and treatment of disease—all this happened in the space of seventy-five years.

As facts became known, investigators and clinicians gradually utilized them in the practice of medicine. Knowledge concerning the prevention and treatment of disease in infancy and childhood increased in the last quarter of the nineteenth century until a few physicians found it feasible to limit their practice to the care of children. The first hospital for children was opened in Philadelphia in 1854; this was followed in 1855 by the opening of the Nursery and Child's Hospital in New York. The child welfare movement was in its infancy during this period. In 1873 Jacobi recommended that cow's milk be cooked before being fed to children. In 1889 the first depot for the distribution of milk to infants was opened in New York city in the Good Samaritan Dispensary. In 1892 Nathan Straus established the first depot for the distribution of pasteurized milk. During this period the infant welfare program was largely the concern of individual physicians and citizens and of a few voluntary agencies. In 1879 the New York state legislature, concerned because of the high infant mortality among the poor in New York city, required the New York City Board of Estimate and Apportionment to appropriate $10,000 for the employment of physicians to visit the tenements during the summer months and treat sick babies. With this exception public authorities took no action to reduce infant deaths until 1897, when the city of Rochester established a municipal infant milk depot, providing the milk from a municipally owned farm. In the next few years infant milk stations were organized in many cities, including Cleveland, Baltimore, Philadelphia and Chicago, and so the public program of infant welfare was launched. The need to provide medical and nursing services at the infant welfare stations and follow-up nursing in the homes soon became apparent, and there gradually emerged the child health conference, at which advice with respect to infant feeding and routine care was given by physician and nurse. Not until some time later, however, was stress to be laid on the antepartum care of the mother and the immediate postnatal care of the infant as essential to the reduction of infant deaths. It is, however, of some interest that the first antepartum conferences were conducted by pediatricians with a view to lowering infant mortality.

In the last decade of the nineteenth century public authorities became concerned with three other aspects of the protection of the health of children. Systems of medical inspection were inaugurated in the schools of a few cities, the production and distribution of diphtheria antitoxin was undertaken by the Department of Health of New York city and by that of the state of Massachusetts, and thirteen states passed legislation concerning the control of ophthalmia neonatorum.

And so at the beginning of the twentieth century conditions were ripe for a steady forward movement in child health, as they had been a century before for progress in public education. Public bodies, largely the municipal authorities, were recognizing that the problems of child health are not limited to any special segment in the population and that such safeguards as pasteurization of milk, school medical inspection and administration of diphtheria antitoxin must be made available for all the people. Public interest was growing steadily, physicians were armed with new weapons against certain diseases, and public health nurses were beginning to take their place in the program. The next two decades were to see rapid increase in knowledge of the extent and causes of infant and maternal mortality and the acquisition of much new knowledge regarding the nutrition of infants and children and their protection against communicable diseases. During these two decades also there began to develop a demand by the people for action on the part of the government that would make this newer knowledge more generally effective in saving lives and promoting health of mothers and children.

What are some of the events of this, the twentieth, century that indicate the growing acceptance of public responsibility for the health of children?

The first outstanding event, perhaps that which most effectively turned the attention of people away from the child health problems of their separate localities to those of the nation as a whole, to the rural mother and child as well as the city mother and child, was the law passed by Congress in 1902 authorizing the Bureau of Census to collect and publish statistics on births and deaths annually. By this act the federal government accepted its first major responsibility in the child welfare program—that of providing the data which still hold first place among indexes of accomplishment in the field of child health. Lemuel Shattuck had recommended in 1845 that infant mortality statistics be based on live births. The first federal infant mortality rates based on live births, however, concern the year 1910. As late as 1907 it was generally recognized that there was no state or city in which registration of births was even fairly complete. The Birth Registration Area, as established in 1915, included ten states and the District of Columbia. Its completion, in 1933, with the admission of the last state at last made possible on a nationwide scale collection of data which are basic evidences of need or progress in the field of maternal and child health.

The census for 1910 showed that 132 infants of every 1,000 born alive during the year died before they were a year old but that under the conditions in certain communities the rate was lower. Voluntary efforts and special demonstrations in cities were showing that infant mortality could be greatly reduced. There was no question in the minds

of those engaged in the movement that infants died unnecessarily. The Committee of One Hundred on National Health had estimated in 1909 that half of the deaths among infants and young children were preventable. The problem was how to make the new educational methods available to all mothers, rural as well as urban.

The years from 1900 to 1912 were notable for the extension of local activities in cities and for the development of national interest.

In 1908 New York city created, as a part of its department of health, the first unit of local government to be concerned solely with the health of children, the Bureau of Child Hygiene, and appointed as director a pediatrician already experienced in child health work. Gradually the bureau took over many of the routine child health services that had been started by voluntary agencies, including infant welfare clinics, prenatal services, control of midwives, supervision of day nurseries and school health services. The establishment of the Bureau of Child Hygiene was followed shortly by inauguration of similar bureaus in other cities, but for years the New York city bureau led the way as a pioneer in the field. School medical inspection and school nursing service developed rapidly during these years. By 1910, four hundred cities had made a beginning in medical inspection.

The Conference on the Prevention of Infant Mortality held under the auspices of the American Academy of Medicine in 1909 and the subsequent formation of the American Association for the Study and Prevention of Infant Mortality brought together from all parts of the country workers interested in the various phases of child life, and a great national stimulus was given to child health activities. At the time of the conference there were bills before Congress calling for the creation of a federal children's bureau that should include within its scope of interest all phases of child life and devote itself to investigating problems that concern the welfare of all children, but it was not until 1912 that the proponents of the measure were successful. By creating the Children's Bureau and giving it investigative functions in the broad fields of health and disease, dependency, delinquency and industrial occupations, Congress expressed its belief in the fundamental responsibility of the federal government for the welfare of the children of the nation. To discharge its investigative functions productively and to make the results effective by reports to the people through a variety of channels have always been the most important objectives of the bureau's staff. In so doing, as in the earliest studies of infant mortality, inaugurated almost immediately after creation of the bureau, it has held that consideration of the social and economic conditions surrounding the lives of children and their effect on health is of utmost importance in the evaluation of needs. Since its creation the Children's Bureau has been

given still broader functions in the field of health as in other fields, not for the purpose of lessening the responsibilities of the states but to enable the federal government to give financial assistance and more effective technical advice and consultation service to the states in their programs of child health and child welfare.

Following the creation of the Children's Bureau, and partly in response to some of its activities, there developed widespread recognition of the responsibility of state governments for the supervision of children's health and for the protection of mothers and infants. In 1914 New York state established a division of child hygiene in the Department of Health, appointed a pediatrician as its director and provided funds to carry on an active campaign to stimulate child health activity in the various localities of the state. Two years previously the state of Louisiana had established a division but had failed to appropriate funds to implement a program. Other states in rapid succession followed New York's example until, by 1922, forty-six states had organized such divisions in their departments of health.

During these same years active debate began on the question of the need for federal grants to states to aid them in developing their maternal and child health activities. Examinations of recruits drafted for the army in 1917 had been highly disillusioning with regard to the health status of the young men. Public support for a plan for federal grants-in-aid to the states, especially support from the women's organizations and from other groups concerned with child health or welfare, finally culminated in the passage of the Maternity and Infancy Act, in 1921. This act authorized distribution of $1,240,000 annually for grants-in-aid to states but limited to five years the period in which the grants could be made. At the end of the five-year period an extension of two years was given, but after this the provisions of the act lapsed. Though the period of operation of the Maternity and Infancy Act was short, opportunity was given to the states, in many cases for the first time, to develop prenatal and child health programs in rural areas; public health nursing was made an important integral part of the child health program; conferences on child health and prenatal clinics were organized in many of the smaller cities and towns as well as in rural counties; school health work was stimulated, and the people of many communities discovered for the first time the advantages of a public program for the supervision of the health of mothers and children. Because the total amounts of money granted to individual states were relatively small, the programs obviously could not be developed in all areas as permanent activities or with local continuing personnel paid for their services. Much of the work was necessarily carried on from the central office of the state division, and state personnel conducted itinerant or demonstra-

tion conferences in the rural areas. Through these procedures the program had wide educational value but served less well in establishing permanent services in the localities. Though at the end of seven years the funds were withdrawn, much of benefit remained. A number of the states increased their appropriations to meet at least part of that which was withdrawn; all the states, even the three that had never accepted federal funds, benefited from the administrative experience involved in the enlarged program, from opportunities for exchange of experience afforded through annual conferences of state directors and in other ways. Though this first attempt of the federal government to promote the health of mothers and children came to an end in 1929, the responsibility of the federal government to aid the states in this respect had been declared, and it was only a matter of time before provision was again made for this type of service on a nationwide basis.

In 1935, after six years of economic depression, the Social Security Act became law; it carried in one of its titles provision for maternal and child health, medical services for crippled children and child welfare services for rural children. For about three years funds have been available for each of these programs. All the states and territories are cooperating in the maternal and child health program, all but one in the program for crippled children and all but one in the child welfare program. The federal funds available for maternal and child health are nearly three times as great as those available under the Maternity and Infancy Act. Because no time limit was set by the Social Security Act, the states have been able to develop programs gradually and with a sense of permanence; careful administrative planning has been possible, and qualified personnel has been selected or "in service" training has been provided.

Under the maternal and child health program there has been increasing indication of acceptance of the principle of public responsibility for maternity care and care of children, and major advances have been made in public understanding as to the functions of state and local governments. This has been clear in the annual plans that the states have submitted to the Children's Bureau for approval. It is apparent that under these plans services are being provided not for selected groups but for women and children for whom such services are not available from other sources. Special attention is given to families in rural areas and in areas of economic distress, where the resources of the community are not sufficient to provide necessary care.

Reports from state departments of health for the year ended June 30, 1938, show that in selected localities, other than the larger cities, twenty-nine states have undertaken special maternity care programs which include care for the mother at time of delivery as well as in the antepartum and postpartum periods. Nearly all the states recognize the

need to provide adequate care at delivery, but few have been able to do more than undertake a special nursing demonstration in a localized area. The provision of a physician's as well as a nurse's care at delivery in the home and payment for hospital care when it is necessary either for medical or for social reasons must be the next steps in the maternity care program. If these were provided, not only would the maternal death rate and the death rate of newborn infants be reduced, but an untold number of women would have better health after childbirth. To make this provision would call for the services of three to four times as many public health nurses as are available today; the services of physicians, both specialists, as consultants, and general practitioners, clinic care, hospital care, transportation to the hospital and household help for the family left behind would need to be provided in many areas and for many women for whom they are not now available. The state health officers have clearly indicated their need for increased funds to provide more adequately for maternity care and care of infants. When submitting to the Children's Bureau their plans for the current year the state health officers of twenty-eight states reported amounts required to meet immediate needs, including medical and nursing care, that totaled approximately $22,000,000 annually in addition to present expenditure.

Child health services, too, have spread rapidly under this new federal-state cooperative program. In 1937 there were 5,700 child health conferences in rural or semirural communities, financed in part from social security funds and in part from state or local funds. In 1938 the state departments of health reported that 1,800 new conferences had been established. And still, at most, in only one third of the rural counties was this type of help available for mothers of infants and young children. State departments of health are placing the responsibility for these child health conferences more and more on the local departments of health, and local physicians are undertaking to provide the medical services in child health and prenatal conferences and clinics. In 1938 some 3,400 local physicians were paid from public funds for the services they rendered, an increase of 25 per cent over the number paid for these services in the previous year. The number of public health nurses serving rural areas has increased considerably under the social security program, but there are still about a thousand counties without a single public health nurse.

Public authorities are coming to realize that if the quality of maternity and child care given by physicians and nurses is to be maintained at a high level provision must be made for continuous supervision of services, for "in service" training and for postgraduate education. Supervision of the medical services by competent pediatricians and obstetricians serving as administrative assistants on staffs of state or local departments of health is not yet well developed, largely because

in many states funds have not been sufficient for their employment. Under the Social Security Act, however, departments of health in forty-four states have made funds available for postgraduate courses in pediatrics and obstetrics offered to general practitioners in rural areas and smaller towns. These courses have been organized with the cooperation of state and local medical societies. The need for short courses in clinical obstetrics and pediatrics at medical centers is becoming apparent. Medical schools of several state universities are experimenting with this type of instruction. Other universities will undoubtedly be called on in the future.

No one today questions the need of any community for the services of specialists in pediatrics and obstetrics as consultants to assist general practitioners in diagnosis and treatment, to serve on hospital staffs and to assist in organizing or managing child health conferences or prenatal clinics. Many areas and districts of this country, however, have no such consultants, and families must either go long distances to obtain such aid or pay large fees for the specialist to come to see them. Many families can do neither. And so it has become apparent that for this type of service also responsibility must fall on the public authorities in many areas.

The development of activities under the Social Security Act has stimulated wide public interest in the maternal and child health program; this has been manifested, among other ways, in the growing use of the device of the advisory committee, professional or nonprofessional. The creation of such committees by public agencies is an attempt to use in the public program the advice and practical assistance of public spirited citizens who for generations in this country have devoted time and effort to voluntary social agencies and who have been responsible in this way for much of past progress in bettering conditions for children. The interest of citizens, both lay and professional, in the public program of child health is essential to its success. It is true that administrative authority for public programs must rest in the duly elected and appointed public officials, but a wise public official knows that without the support of the people of his community he cannot most effectively carry forward the program under his charge. It is the responsibility of the people to devise the safeguards necessary for the selection and appointment of competent, qualified public administrators and other personnel. The use of advisory committees of citizens and of technical committees of professional experts to make recommendations to the public agencies, especially with regard to standards of service, and in turn to interpret the public program to the people is a procedure that needs wider consideration and trial than is given it today. The establishment of merit systems for the selection of professional as well as nonprofessional personnel

for the health services, from the highest administrative officials down, is of paramount importance to the future of the program. There is still much that professional associations and other voluntary organizations can do to strengthen the state and local health services by establishing the principle of the merit system and insisting on high standards of service.

It seems evident that the next few years will see expansion of the health services to include medical care of the sick. The child health program, because of its essentially clinical nature, can be adapted without great difficulty to include medical care of sick children. Today the general practitioner gives, and I believe that under an expanded program he will continue to give, the largest amount of medical service to mothers and children. The community, through its official health agency, will continue to carry responsibility for organization and administration and for the quality and economy of the service rendered.

Under the Social Security Act provision has already been made for one special type of service that is primarily medical care of the sick, the program of care for crippled children. The state plans submitted each year to the Children's Bureau provide for locating crippled children and for medical, surgical and hospital care with the after-care necessary to insure satisfactory rehabilitation of the child. The federal grants-in-aid to the states for this purpose have made possible the development of administrative procedures in the states and administrative relations between the states and the federal government that are susceptible of adaptation to a future program of general medical care for children or to a maternity care program financed through grants-in-aid. Under the crippled children's program administrative policies have been slowly emerging with respect to the use of public funds for the care of children in need of the service. These policies have involved such matters as the choice of the state agency best adapted to the administration of a program of medical care, the maintenance of a high quality of medical, surgical and hospital care and the organization of services necessary to insure adequate attention to the social problems involved in the provision of good care and health supervision in the home of the child. Many problems relating to authorization for care, of determination of eligibility for care, methods of payment of physicians and of hospitals and use of public or of nonprofit voluntary hospitals have been considered by the states and by the Children's Bureau in conference with the state administrators or by special advisory committees of experts in the care of crippled children. The experience that has thus been acquired will be of the greatest value in any expanding program of medical service.

The need for an expanding program of medical care need not be dwelt on here. The immediate response to the National Health Conference called last July at the President's suggestion by Miss Roche, chairman of the Interdepartmental Committee to Coordinate Health and Welfare Activities, the continuing intense interest of the people expressed through the daily press and magazines and through resolutions of organizations representing large groups, the desire for information and for conferences on the part of leading professional groups of the country, not to query the need for increased public service but to discuss how it shall be met, leave little doubt as to public support for a national health program. It is significant that the first recommendation of the Technical Committee on Medical Care (of the Interdepartmental Committee) was expansion of the public health and maternal and child health programs to include certain phases of medical service to the sick. In the expansion of the maternal and child health program, the recommendations call not only for additional funds for promoting health of mothers and children but for a major extension of the program involving payment for physicians' services, hospital care, and other services necessary to provide for women throughout the maternity cycle and for sick children. The inclusion of these medical services in the first recommendation that relates to general public health can be interpreted only as meaning that in the opinion of the committee maternity care and complete health services to children are matters of such broad social and economic significance that the needs must be met by the nation as a whole and be provided to the nation as a whole on the same broad basis as public health.

It has been well said that "the sources of revenue must be as broad as the causes of need." In the field with which the Children's Bureau is concerned the causes of need are indeed broad. Each year more than 2,000,000 births take place in this country. Thus there exists a problem of medical care that, unlike any other, is "inevitably premanent." At all times some 35,000,000 children under 16 years of age are going through the process of growth and development that they may be the citizens of the future. Acceptance of public responsibility for the health of these future citizens has been slow in developing, but today it appears to be the most promising point of social advance.

News and Comment

GENERAL

Child Health Day, Monday, May 1, 1939.—The May Day celebration is sponsored, as usual, by the Children's Bureau of the United States Department of Labor. The slogan is "The health of the child is the power of the nation." The object is to bring to the attention of each community the importance to the child's health, development and well-being throughout life of proper food, rest, exercise, medical care and protection against disease; the ways of informing parents and others how child health may be safeguarded, and the means whereby such safeguards may be made available for all children.

Harvey Society Lecture.—The fifth Harvey Society Lecture of the current series at the New York Academy of Medicine will be delivered by Dr. Edwards A. Park, professor of pediatrics at the Johns Hopkins University School of Medicine. The subject will be "The Pathology of Rickets with Particular Reference to the Changes at the Cartilage Shaft Junctions of the Growing Bones."

American Board of Pediatrics.—The American Board of Pediatrics will hold examinations on November 14 and 15, in Cincinnati, preceding the annual meeting of the American Academy of Pediatrics. Appointments for this examination must be made before July 14, 1939.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

Demonstration of Plasma-Anticoagulant in Exudates of Bacterial Origin. E. Neter, J. Infect. Dis. **63**:193 (Sept.-Oct.) 1938.

Exudates associated with bacterial infection may inhibit the coagulation of human plasma. The purulent exudates tested comprised human spinal, empyema and peritoneal fluids, as well as contents of abscesses. The micro-organisms recovered from such anticoagulation exudates were Streptococcus haemolyticus, Streptococcus faecalis, Staphylococcus, Pneumococcus, Haemophilus influenzae, Bacillus coli and Bacillus welchii.

Human pneumococcic exudates contained anticoagulant less frequently than those in which enterococci were present. Exudates due to the presence of the hemolytic streptococcus may contain either anticoagulant or fibrinolysin or both—or such exudates may lack fibrinolytic, as well as anticoagulating, properties.

Toomey, Cleveland.

Effect of Splenectomy and Blockade on the Protective Titer of Antiserum Against Trypanosoma Equiperdum. L. R. Kuhn, J. Infect. Dis. **63**:217 (Sept.-Oct.) 1938.

The protective titer of anti–Trypanosoma equiperdum sheep serum is appreciably reduced after being injected intraperitoneally into mice provided the mice have been splenectomized and blockaded with india ink or normal serum and treated with subcutaneous injections of from 2,500 to 3,000 trypanosomes, but it is not reduced if the mice have been only splenectomized or if the mice have been splenectomized and blockaded with specific, i. e., anti-T. equiperdum sheep serum. Furthermore, it is only slightly reduced in mice splenectomized and blockaded with india ink and treated with subcutaneous injections of from 1,200 to 1,600 trypanosomes. Splenectomy plus blockade appears to have no effect on the resistance of mice to trypanosomes specifically sensitized in vitro. The effect of splenectomy and blockade on the protective titer of trypanocidal serum cannot, therefore, be due to inhibition of phagocytosis, decrease in complement or reduction of opsonin, but it may be due to interference with the concentration of passively acquired antibodies in macrophage tissues.

Toomey, Cleveland.

Metabolism; Infant Feeding; Milk and Other Foods

Effect of Growth on the Distribution of Water and Electrolytes in Brain, Liver and Muscle. H. Yannet and D. C. Darrow, J. Biol. Chem. **123**:295, 1938.

The effect of growth on the chemical composition of the brain, liver and muscle was studied in cats of different ages. In the brain, growth is associated with a decrease in the concentration of water, sodium and chloride and an increase in the concentration of fat, phosphorus and nitrogen. These changes are related to the growth of the body as a whole, according to Huxley's "constant differential growth ratio." Anatomically, the changes are brought about chiefly by the deposition of lipid in the myelin sheaths, associated with a decrease in the proportion of extracellular fluid. In muscle, growth is associated with a decrease in the concentration of sodium and chloride and an increase in the concentration of nitrogen, phosphorus and potassium. There is little change in the percentage of

total water. These changes in chemical composition represent a change in the distribution of water between the intracellular and the extracellular compartments resulting from the growth of the muscle fibers. The relation of the increase in the percentage of intracellular fluid and the decrease in the percentage of extracellular fluid to the growth of the body as a whole also follows the "constant differential growth ratio." The livers of the older animals show an increased concentration of lipids, phosphorus and nitrogen and a decreased concentration of sodium, chloride and water. These changes are apparently all associated with the deposition of lipid and are related to the nutritional status of the animals rather than to growth. Except for a decrease in the concentration of intracellular potassium in the livers of the older animals, no changes are demonstrated in the concentration of nonlipid nitrogen, nonlipid phosphorus or potassium in the intracellular fluid of the tissues studied.

PAGE, Indianapolis. [ARCH. NEUROL. & PSYCHIAT.]

THE MILK SUPPLY. A. S. MACGREGOR, Edinburgh M. J. **45**:363 (May) 1938.

Macgregor contributes a short article on the safeguarding of the milk supply for such cities as Glasgow, Scotland, by the production of milk free from tubercle bacilli and pasteurization against other infections. He insists that milk firms which receive raw milk from various farms should be prohibited from mixing and distributing this without pasteurization, whether or not it originated from tubercle bacillus-free herds. It is unsound to exempt tubercle bacillus-free milk from compulsory pasteurization in a large center of population.

NEFF, Kansas City, Mo.

DIETETIC NOTIONS AND THE ALIMENTATION OF PREGNANT AND OF NURSING WOMEN. A. MAROTTA, Prat. pediat. **16**:99 (April) 1938.

This is an elementary discussion of the subject, largely empiric in its approach.

DOOLEY, New York.

MIXED FEEDING. H. CESTANEDA, Rev. mex. de puericultura **8**:151 (Feb.) 1938.

Cestaneda discusses the general principles of infant feeding and suggests that the weight rather than the age, the tolerance rather than the theoretic amount the baby should get, be used as guides in infant feeding.

HERRON, Monroe, La.

Vitamins; Avitaminoses

DERMATOLOGIC SYMPTOMS OF VITAMIN DEFICIENCIES. H. GOODMAN, Arch. Dermat. & Syph. **38**:389 (Sept.) 1938.

The characteristics of cutaneous lesions observed in experimental work with animals and in clinical practice with human beings which have been considered due to a lack or to an excess of the individual vitamins are outlined from the available literature and from the author's own experience. An extensive bibliography is given.

JACKSON, Iowa City.

RED PALM OIL IN THE TREATMENT OF HUMAN KERATOMALACIA. W. R. AYKROYD and R. E. WRIGHT, Indian J. M. Research **25**:7 (July) 1937.

Aykroyd and Wright determined the vitamin A activity of red palm oil by experimentally producing in rabbits a condition resembling clinical keratomalacia and then curing the lesions by giving each rabbit from 0.5 to 2 Gm. of red palm oil. After that they carried out a clinical trial, using 10 minims (0.6 cc.) of the

oil, in an emulsion, as an average dose for children between 5 and 10 years of age, a suitable alteration being made for younger and older patients. This dose was given twice daily. Difficulties were encountered, one of which was the possibility that the beneficial effects may have resulted simply from admitting the patients to the hospital and placing them on a balanced diet. In 3 instances, however, the authors were able to treat and follow up patients suitable for observation who remained living under the identical domestic conditions in which the syndrome developed. The only change in their daily routine was the addition of an emulsion of red palm oil to their diet. In these the improvement was so definite that the investigators concluded that so far as the strictly limited observation went the red palm oil alone acted in a curative capacity, supplying the necessary factor or factors in the same way as cod liver oil had done in the past. Most of the patients with keratomalacia treated in the hospital were infants and young children. Cessation of deterioration was observed within a week and definite improvement within a fortnight after the commencement of treatment with the red palm oil. Seven samples of cod liver oil averaged about 300 micrograms of vitamin A per gram, while three samples of red palm oil averaged about 500 micrograms of carotene per gram. Most of the samples of cod liver oil were obtained by local purchase. As estimated by De's method, 1 microgram of carotene and 1 microgram of vitamin A are roughly equivalent to 1 and 2.6 international units, respectively. ZENTMAYER. [J. A. M. A.; ARCH. OPHTH.]

EXPERIMENTAL STUDIES ON THE PHYSIOLOGY OF VITAMIN A. W. CATEL, Monatschr. f. Kinderh. **73**:316 (June) 1938.

A great number of experiments were conducted on various animals and on infants to gather further information regarding vitamin A. Vitamin A was determined in milligrams of carotene. It was found that the vitamin A content of venous blood is dependent on the food, the season and the age of the subject. Only when the content of the patient's blood varies decidedly from the general average, the age and season being taken into consideration, should one speak of a deficiency.

In premature infants the level of vitamin A in the serum can be raised fifty times by forced feeding; but after about four weeks it remains constant or even falls.

In regard to keratomalacia, Catel believes vitamin A deficiency is not the sole factor.

In a child with thyrotoxicosis the low level of vitamin A in the blood could be raised without influencing the clinical picture.

During the winter season raw breast milk contains 0.4 mg. of vitamin A per hundred cubic centimeters.

Healthy persons excrete vitamin A in the urine in amounts varying from 0.02 to 0.2 mg. per hundred cubic centimeters.

Vitamin A or its split products may be identified in the urine by the development of a yellow-brown color on addition of antimony trichloride.

Metabolism experiments suggest that forced feeding of vitamin A does not lead to increased retention; the vitamin is excreted in another form through the urine or bile. GERSTLEY, Chicago.

THE ANTIRACHITIC VITAMINS. H. BROCKMANN, München. med. Wchnschr. **84**: 1939 (Dec. 3) 1937.

Brockmann reviews some of the outstanding achievements which led to the chemical isolation of the antirachitic vitamins. In 1890 Palm observed the relation between the geographic distribution of rickets and the intensity of the sun's rays. Mellanby produced rickets experimentally in dogs and rats in 1918 by feeding them a special diet. Shortly afterward Huldschinsky demonstrated that rickets

could be cured by ultraviolet rays. In 1924 both Hess and Steenbock showed that certain foods could be made antirachitic by irradiating them with ultraviolet rays. It was soon found that animal and human skin contained a provitamin and that vegetable sterols and cholesterol became antirachitic when they were irradiated. Hess and Windaus showed that ergosterol was an antirachitic provitamin.

Many contributions have been made in attempts to isolate chemically pure vitamin D. In 1932 Windaus and his co-workers isolated two substances after irradiating ergosterol, which were termed vitamin D 1 (lumisterol) and vitamin D 2. Vitamin D 2 was a chemically pure antirachitic vitamin. A crystalline substance isolated by Bourdillon in England was called calciferol. Later it was found that this was a mixture of vitamin D 2, lumisterol and other substances. At present the name "calciferol" designates pure vitamin D 2. Windaus established the structural formula of vitamin D 2 and was able to clarify the chemical changes which occurred when ergosterol was irradiated. Ergosterol is first changed into lumisterol (a stereoisomer of ergosterol), and then by a change in the bonds between two of the carbon atoms vitamin D 2 is formed.

Experiments by Windaus and his co-workers showed that irradiation of 22-dihydroergosterol produced another antirachitic substance, which they named vitamin D 4. This substance is somewhat less effective than vitamin D 2 in the rickets of rats but is more effective in the rickets of chickens. Furthermore, it was found that irradiation of 7-dehydrocholesterol produced still another antirachitic substance, named vitamin D 3. Its antirachitic potency is the same as that of vitamin D 2 in rats but thirty times greater than that of vitamin D 2 in chickens.

The vitamin in cod liver oil is apparently not identical with vitamin D 2, since the former is more effective in the rickets of chickens. The vitamin in tuna fish oil is identical with pure vitamin D 3. Vitamin D 3 is twice as effective in the rickets of man as vitamin D 2.

Following the discoveries of several antirachitic vitamins the identification of the natural provitamin in animals was again undertaken. Previously it had been thought to be ergosterol. However, Windaus and Bock showed that the provitamin in the skin of man and most animals was 7-dehydrocholesterol, which after irradiation produced vitamin D 3.

BRAHDY, Mount Vernon, N. Y.

EFFECT OF ULTRAVIOLET RAYS ON THE VITAMIN C CONTENT OF MILK. H. SCHROEDER, Münchcn. med. Wchnschr. **84**:1942 (Dec. 3) 1937.

Schroeder studied the effect of ultraviolet rays on the vitamin C content of plain milk and of milk enriched with ascorbic acid, orange juice and other fluids containing vitamin C, as well as on an aqueous solution of ascorbic acid. A 3 to 5 mm. layer of each fluid to be examined was placed in a Petri dish and maintained at a temperature of 0 C. at a distance of 25 cm. from a mercury vapor lamp. At various intervals over a period of one or two hours the vitamin C content of the fluids was determined by the Tillman method. The ultraviolet rays destroyed the vitamin. The same fluids exposed to the light from an ordinary 25 watt bulb showed no loss of vitamin C.

BRAHDY, Mount Vernon, N. Y.

Hygiene; Growth and Nutrition; Public Health

THE DOCTOR AND A SCHOOL HEALTH PROGRAM. H. COOK, J. Michigan M. Soc. **37**:593 (July) 1938.

Cook, speaking at a joint meeting of the extension division of the University of Michigan and the Michigan School Health Association, clearly set forth the relationship of the physician to the health program in the school. His pronouncements may be considered those of organized medicine in Michigan.

In brief, he urged that the program be discussed with local physicians before its inception, in order that there may be a thorough knowledge of its aims and objectives, that cooperative effort may be secured and that the whole program may be carried out "on a strictly ethical basis." CAREY, Detroit.

CONTROL OF INFECTION IN CHILDREN'S WARDS. R. H. DOBBS and R. KEMPTHORNE, Lancet **1**:1373 (June 18) 1938.

The purpose of this article is to indicate how the incidence of infection in children's hospitals can be reduced. It is admitted that infection cannot be entirely eliminated.

Careful technic at the time of admission (isolation of the incoming patient during the first forty-eight hours) will greatly reduce the number of initial infections and careful technic in the wards will greatly reduce their spread. It is important that immediately on discovery of a rise of temperature or on a complaint of sore throat the subject, whether a patient or a staff member, should be isolated.

Speaking of hemolytic streptococcic infections, the authors emphasize that the dangerous carriers are those from whom streptococci of group A are isolated in heavy growth and who have unhealthy throats or discharges containing these organisms.

As far as measles is concerned, they suggest that it is more reasonable to allow the occurrence of measles in wards throughout epidemics, removing each patient in whom measles develops, than to waste valuable beds through repeated closure and disinfection of wards.

No member of the staff can be sufficiently indispensable to justify risking the consequences of an epidemic of a respiratory infection. The staff member with a common cold must be excluded during the infectious period of his ailment and must take no part in the preparation of food. Nurses destined for duty in the children's ward should be given instruction in the elements of infection and immunity.

Visitors should be allowed to see only children who are seriously ill, and then only if the visitors are free from infection and if a gown is worn.

LANGMANN, New York.

CENTERS FOR THE COLLECTION OF HUMAN MILK. E. MEYNIER, Lattante **9**:261 (June) 1938.

Meynier gives a historical review of the establishment in Italy of centers for the collection of human milk. He urges the installation of new centers.

HIGGINS, Boston.

BIOMETRIC DATA ON THE NEWBORN IN FERRARA. A. GALANTE, Lattante **9**:284 (July) 1938.

Biometric data on 173 newborn infants of Ferrara, Italy, are recorded. The data are compared with those from other districts in Italy.

HIGGINS, Boston.

STATISTICAL INVESTIGATIONS FROM 1901 TO 1937. F. AUXILIA, Lattante **9**:385 (Sept.) 1938.

Auxilia has found that the number of illegitimate infants per year coming under the care of the Institute for the Protection of Infants in the province of Savona has diminished from 76 to 40 since 1901. Before the world war the death rate of infants in the first year of life was 231 per thousand illegitimate children and 149 per thousand legitimate children. During the last decade the death rate of illegitimate children was 71 per thousand. HIGGINS, Boston.

IS THE COUNTRY DOCTOR IN NEED OF AN ASSISTANT? ABRICOSSOFF, Rev. méd.-sociale de l'enf. **5**:355 (Sept.-Oct.) 1937.

With no attempt at eulogizing, Abricossoff points out the varied demands made on the country doctor and particularly stresses the amount of time and energy that he must expend on problems that could be solved by nonmedically trained persons. Although the physician's wife may assume some of his nontechnical duties, it is the author's conviction that some regular provision for an aid should be made. Many of the problems of prenatal and postnatal hygiene, control of tuberculosis, education in preventive medicine, school adjustment and even old age could well be cared for by a nonmedical assistant working as an ally rather than as a rival of the country doctor.

DIETRICH, Beverly Hills, Calif.

THE PRENATAL CLINIC. O. SOUZA, Bol. Inst. de puericultura, Rio de Janeiro **1**: 51, 1938.

The author reviews the requirements of such a clinic.

SANFORD, Chicago.

INTERPRETING THE WEIGHT CURVES OF INFANTS. R. DE LAMARE, Bol. Inst. de puericultura, Rio de Janeiro **1**:119, 1938.

De Lamare tabulates the results published by several authors, showing that there is no agreement as to the normal gain in weight of children in the first year.

SANFORD, Chicago.

Prematurity and Congenital Deformities

SIGNIFICANCE OF PREMATURE BIRTH IN THE DEVELOPMENT OF CEREBRAL DEFECTS, WITH ESPECIAL REFERENCE TO EXOGENOUS FACTORS CAUSING VARIOUS DEGREES OF MENTAL DEFICIENCY. T. BRANDER, Acta psychiat. et neurol. **12**:313, 1937.

The problem of the mental development of the prematurely born infant is of practical importance. About 10 per cent of all newborn infants are premature, and about half of them survive to reach school age. They represent 5 per cent of all school children. Brander studied the intelligence quotient in relation to various endogenous and exogenous factors influencing the intellectual development of prematurely born infants, such as weight at birth, birth trauma and psychopathic heredity. His material consisted of 376 prematurely born children between 7 and 15 years of age. His findings were as follows: The average intelligence quotient of premature children is definitely lower than that of a nonselected group of children of the same age. Birth trauma and psychopathic heredity tend to lower the intelligence quotient. The two factors in combination have an unfavorable effect on the intelligence quotient of premature children at school age. Psychopathic heredity alone has a more unfavorable effect than birth trauma alone. Thus, of a group of 230 premature children without birth trauma and without psychopathic heredity, 57.4 per cent were normal (intelligence quotient from 120 to 91), and 4.3 per cent were feebleminded (intelligence quotient 70 or below). Of a group of 66 premature children with complications at birth, 34.8 per cent were normal, and 13.6 per cent were feebleminded; of a group of 54 premature children with psychopathic heredity, 29.6 per cent were normal, and 24.1 per cent were feebleminded; of the group of 20 premature children with both birth trauma and psychopathic heredity, 30 per cent were normal, and 35 per cent were feebleminded. A study of the relation between weight at birth and the intelligence quotient in a group of 230 premature children without trauma at birth and without psychopathic heredity showed that the lower the weight at birth the lower was the intelligence quotient at school age. The average weight

at birth, 2,300 Gm., corresponded to an average intelligence quotient of 92; a weight of 2,200 Gm., to an intelligence quotient of 90; a weight of 1,900 Gm., to an intelligence quotient of 85, and a weight of 1,400 Gm., to an intelligence quotient of 77. Of complications at birth, face and breech presentations and precipitous delivery were most unfavorable. Low forceps delivery, asphyxia, moderate dystocia and protracted delivery seemed to have no influence on the intelligence quotient, but any combination of these complications was reflected immediately in a lower average intelligence quotient at school age. Trauma at birth has a more definitely unfavorable effect on the mental level of premature children than weight at birth alone. Breech presentation was associated with a lower average intelligence quotient than normal delivery of infants of the same weight, and in the cases of breech presentation children delivered by version or by forceps showed a lower intelligence quotient than those of the same weight who were delivered without these procedures. As to the role of psychopathic heredity, nonsyphilitic psychoses in antecedents showed no influence on the intelligence quotient. The occurrence of epilepsy was definitely unfavorable. Alcoholism was most unfavorable. Of a group of premature children with a history of alcoholism in the antecedents, 38.7 per cent were feebleminded. The author concludes that mental deficiency in the prematurely born infant is the result of the action on the nervous system of several endogenous and exogenous factors. Some of these factors are preventable, especially trauma at birth. Brander emphasizes the importance of prophylaxis at birth in preventing or reducing potential mental deficiency in the premature child.

YAKOVLEV, Waltham, Mass. [ARCH. NEUROL. & PSYCHIAT.]

Newborn

ANEMIA AND JAUNDICE IN THE NEW-BORN. W. M. WHITAKER, Illinois M. J. **74**:134 (Aug.) 1938.

In this rather comprehensive article Whitaker discusses the relationship between congenital hydrops, icterus gravis, anemia of the newborn and fetal erythroblastosis, on one hand, and the various clinical syndromes associated with jaundice, on the other. He presents case histories illustrating his points.

BARBOUR, Peoria, Ill.

FEEDING OF FULL TERM INFANTS DURING THE NEW-BORN PERIOD. G. M. CLINE, Illinois M. J. **74**:142 (Aug.) 1938.

In this article Cline discusses the various factors important for successful feeding of infants. He emphasizes the prime importance of breast milk.

BARBOUR, Peoria, Ill.

FEEDING IN THE NEWBORN. J. M. BATY, M. Clin. North America **22**:829 (May) 1938.

Baty advises putting the baby to the breast within from twelve to twenty-four hours after birth, with six hour feeding intervals for the next twenty-four hours and four hour intervals thereafter. He does not favor prelacteal feedings except of water or simple sugar solutions. For supplemental feeding later and for the feeding of those infants who are entirely bottle fed, simple milk and sugar mixtures, beginning with weak dilutions, may be safely used as a routine.

EUGENE H. SMITH, Ogden, Utah.

MATERNAL AND NEONATAL CARE. F. L. ADAIR, M. Rec. **147**:22 (Jan. 5) 1938.

This interesting educational article is recommended for perusal. Adair calls attention to sociologic problems in maternal and infant care and urges that phy-

sicians take a leading part in the solution of medicosocial problems in their communities. He commends, the Maternal Welfare Committee on their moving picture, "The Birth of a Baby." Hereditary factors are discussed under the heading "Preconceptional Care," emphasis being laid on the importance of premarital examination. "The only prophylaxis for venereal disease in women is the selection of healthy mates."

Of particular interest to the pediatrician in this article is the part on the care of the newborn. He condemns rough treatment in resuscitation of the newborn, recommending the use of warmth, oxygen and a little carbon dioxide.

WESTON JR., Columbia, S. C.

CALCIUM STUDIES IN THE NEWBORN. B. S. DENZER, M. REINER and P. VOGEL, Proc. Soc. Exper. Biol. & Med. **39**:492 (May) 1938.

The calcium level in the blood of 47 newly born infants tended to be lower during the first four days after birth than that in blood from the umbilical cord, with a gradual rise to the prenatal level during the next five days.

HANSEN, Minneapolis.

INTRACRANIAL HAEMORRHAGE IN THE NEW-BORN. W. S. CRAIG, Arch. Dis. Childhood **13**:89 (June) 1938.

A study was made of a series of 126 infants in whom intracranial hemorrhage was found post mortem. The clinical observations which had begun with birth, and the pathologic changes noted at autopsy are given. The cases are grouped, and the clinical and pathologic observations in connection with them are recorded according to the distribution of the intracranial bleeding. Subdural hemorrhage was present in 62 infants, subarachnoid hemorrhage in 36, intraventricular hemorrhage in 22 and hemorrhage into the brain substance in 6. In general, subdural hemorrhage was associated with tearing of the tentorium, maturity and instrumental delivery; subarachnoid and intraventricular hemorrhage, with prematurity and with illness of the mother during pregnancy, and hemorrhage into the brain substance, with prolonged labor and with delivery of a mother of a large first-born child at one or the other extreme of the reproductive period. Intracranial hemorrhage occurred as a manifestation of a hemorrhagic diathesis in only 4 of the infants. It is suggested that toxemia or infection (or both) of the mother during pregnancy is a factor of primary etiologic importance in cases of intraventricular hemorrhage, and that the risks of cerebral hemorrhage associated with forceps delivery are increased when delivery is preceded by manual or instrumental rotation of the head. The diagnosis of intracranial hemorrhages is discussed, and the value of physiognomic diagnosis is emphasized. Importance is attached to an anxious expression, to restlessness of mind rather than of body and to "sponginess" rather than tension or bulging of the fontanel, as early and reliable diagnostic signs. It is considered that, although not always present, adder-like protrusion of the tongue occurs only in infants with intracranial hemorrhage. The clinical pictures associated with the different types of intracranial hemorrhage are compared. Attention is drawn to the indefiniteness and frequent absence of clinical signs in infants with subarachnoid hemorrhage; to the successive periods of improvement, irritation and depression in those with subdural hemorrhage; to the sudden onset, violent symptoms, short course and terminal hyperpyrexia in those with intraventricular hemorrhage, and to the prolonged course, the uninterrupted, progressive fall in weight, the association of mental restlessness with extreme physical weakness, the low body temperature and the insidious decline characteristic of infants with hemorrhage into the brain substance. The frequency with which intracranial bleeding is associated with other pathologic conditions is emphasized. Pneumonia, intrapulmonary hemorrhage and superficial infections together or separately are described as common; urinary

infection is related to the etiologic background of intracranial hemorrhage; the scanty urinary output associated with cerebral hemorrhage favors infection of the urine.

KELLY, Milwaukee.

STERCORACEOUS PERITONITIS IN THE NEWBORN FROM PERFORATION IN THE LARGE INTESTINE AT THE LOCATION OF A CONGENITAL ABNORMALITY. A. BOLLETTINO, Lattante **9**:275 (July) 1938.

A seemingly normal baby passed meconium on the first day and normal stools on the third day. On this day, however, the abdomen began to enlarge. The child became febrile and died within twenty-four hours. The clinical diagnosis was peritonitis. At autopsy this peritonitis was found due to perforation of an ulcer in the transverse colon. The transverse colon at this point showed congenital agenesis of the muscle layers.

HIGGINS, Boston.

PYOPNEUMOTHORAX IN A NEWBORN INFANT. J. J. ALBERTS, Maandschr. v. kindergeneesk. **7**:211 (Feb.) 1938.

This is a description of the case of an infant 4 days old with pyopneumothorax and sepsis. A brief review of the reports of 3 other cases in the literature is given. At necropsy gangrenous pneumonia of the lower lobe of the right lung was found, probably aspiration pneumonia. The mother died on the fifth day after the delivery, from sepsis; the child died the same day.

VAN CREVELD, Amsterdam, Netherlands.

Acute Contagious Diseases

PATHOGENESIS OF ENCEPHALITIS OCCURRING WITH VACCINATION, VARIOLA AND MEASLES. K. H. FINLEY, Arch. Neurol. & Psychiat. **39**:1047 (May) 1938.

Finley presents evidence to prove that the specific allergic state of the body resulting from vaccination influences the central nervous system as well as the skin and other organs. The tissue response to the antibody-antigen reaction in the central nervous system coincides with similar cellular responses to the antibody-antigen reaction known to occur in other parts of the body.

Between the pathogenesis of measles and that of vaccination similarities exist. In the incubation period of encephalitis from smallpox and vaccination there is a similarity to the incubation period of the rash and encephalitis following measles.

Encephalitis following infection of the upper part of the respiratory tract cannot be distinguished pathologically from that following measles, smallpox and vaccination. It occurs after from ten to fourteen days. Finley feels that the response of the central nervous system to the viruses producing these conditions is allergic, the incubation period of the encephalitis corresponding to that of the particular exanthem with which it occurs. The lateness of development of the encephalitis in some cases may be explained by the fact that one cannot observe changes in the central nervous system as in the skin, and the changes go on before there are physical signs.

BEVERLY, Chicago.

USE OF CONVALESCENT SCARLET FEVER AND MEASLES SERA IN PROPHYLAXIS AND THERAPY. W. THALHIMER, Bull. New York Acad. Med. **14**:361 (June) 1938.

In this paper Thalhimer presents his experiences with convalescent serum in the treatment of patients with measles and scarlet fever. If one may judge from the case histories and charts presented, this form of therapy has a definite place in the treatment for these two treacherous diseases. It favorably modifies the clinical course and reduces the complications.

JAHR, Omaha.

FATALITY RATES IN CEREBROSPINAL MENINGITIS. G. WALSH, J. A. M. A. **110:** 1894 (June 4) 1938.

Fatality rates for cerebrospinal meningitis are recorded here covering 23,685 cases in twenty-two cities. The rates were found to vary from year to year, were greatest in children and older people and averaged around 50 per cent. Serum treatment has not altered the mortality appreciably.

HEERSMA, Kalamazoo, Mich.

DURATION OF SMALLPOX IMMUNITY. D. T. LOY and M. W. HUSBAND, J. A. M. A. **111:**781 (Aug. 27) 1938.

About one thousand students entering Kansas State College were vaccinated, and the results were recorded in the same manner as the results reported for the previous year. The results were very similar, indicating that about two thirds had some susceptibility to smallpox. Only 6 per cent had been vaccinated more than once previously. There were 20 per cent more persons completely immune among those who had their last vaccination within five years than among those whose last vaccination occurred longer than five years previously. Also there were 20 per cent more persons completely immune among those who were vaccinated more than once than in the group vaccinated once previously.

HEERSMA, Kalamazoo, Mich.

TREATMENT OF SCARLET FEVER WITH SPECIFIC ANTITOXINS OF LOW PROTEIN CONTENT. J. A. TOOMEY and C. S. BAKER, J. Pediat. **12:**439 (April) 1938.

In a series of 283 patients treated with scarlet fever antitoxin 38.5 per cent had reactions. Recently three different biologic laboratories have produced purified and concentrated scarlet fever antitoxins. This paper is a report on these three products, with regard to serum reactions. In the study, 800 persons were treated with antitoxin I, 92 with antitoxin II and 30 with antitoxin III. The reaction rate following the use of antitoxins I and III was decidedly decreased as compared with the high rate following the use of the old type of scarlet fever antitoxin. Antitoxins I and III were also found to be more potent than antitoxin II.

RAUH, Cincinnati.

POLIOMYELITIS OCCURRING TWO YEARS AFTER VACCINATION AGAINST THE DISEASE: REPORT OF A CASE. L. C. ROSENBERG, J. Pediat. **12:**507 (April) 1938.

In July 1935 a 2 year old child was given three injections of Kolmer's vaccine in dosages advocated for children of standard weight. In July 1937, two years later, the child contracted acute anterior poliomyelitis. Of the 10,725 persons who received Kolmer's vaccine in 1935, this is the first one to acquire the disease. From the reports of many investigators engaged in research on poliomyelitis, all the response one can expect from the injections of the attenuated virus of poliomyelitis appears to be chiefly humoral and not a genuine specific increase in tissue resistance. They agree almost uniformly that the artificial production of neutralizing antibodies in the blood does not confer immunity. In Schultz's opinion the real basis of immunity to poliomyelitis is not humoral but entirely or largely a cytoplasmic modification of previously susceptible neurons. The failure of humoral antibodies in the blood to protect against the disease is due to the fact that the virus normally gains entrance to the central nervous system by way of the olfactory nerves. The terminals of these nerves lie free on the nasal mucosa and therefore probably are out of reach of these substances circulating in the blood and cannot be affected by them. When the virus has been subjected to the action of various physical or chemical attenuating agents in an effort to make it safe for human use, even the humoral response obtained with it is weak, to say nothing

of the failure of tissue resistance to increase. It is evident that the induction of active immunity by the injection of such attenuated virus is a doubtful possibility. Furthermore, it has been shown that the injections are not free from danger.

RAUH, Cincinnati.

GENERALIZED VACCINIA AND ECZEMA VACCINATUM. C. F. MCKHANN and R. A. Ross, M. Clin. North America **22**:785 (May) 1938.

Generalized vaccinia is the term applied to a generalized eruption following vaccination, which occurs most frequently in debilitated subjects suffering from some cutaneous disease. Eczema vaccinatum follows accidental vaccination in patients suffering from some skin involvement, most commonly eczema but occasionally intertrigo, impetigo and secondary syphilis. Both types of disease are to a certain extent preventable if care is exercised in vaccinating persons predisposed to the occurrence of such complications and if those suffering from some eruption, such as eczema, are prevented from infecting themselves.

The period of incubation of generalized vaccinia varies from four to thirty days. Successive crops of lesions may occur over a period of two or three weeks.

In eczema vaccinatum the onset occurs between nine and twenty-three days after contact. While direct contact with a vaccinated area is perhaps the usual mode of infection, experimental evidence has been offered showing the possibility of droplet infection. Vaccine virus has been isolated from the throats of vaccinated persons on the fourth and fifth days after vaccination. After infection, an exacerbation of the underlying cutaneous disease usually precedes the characteristic eruption. Rarely do the lesions remain limited to the previously injured areas of skin.

The course of the disease in both of these conditions is usually mild, although there may be several considerable elevations of temperature lasting from seven to ten days. Occasionally the cutaneous lesions may assume the severity and gravity of malignant variola.

While these diseases are not of frequent occurrence, only under exceptional circumstances is it advisable to vaccinate a debilitated person suffering from a cutaneous disease, acute or chronic, or from an acute or debilitating disease. The infant and the young child with eczema should also be carefully guarded from contact with recently vaccinated persons. EUGENE H. SMITH, Ogden, Utah.

EFFECT OF A STIMULATING DOSE OF PERTUSSIS VACCINE ON CHILDREN PREVIOUSLY IMMUNIZED. JUI-PING WU and FU-T'ANG CHU, Proc. Soc. Exper. Biol. & Med. **39**:693 (June) 1938.

Five infants were given vaccine of Haemophilus pertussis after the procedure of Sauers and when the agglutination titer of their blood had begun to drop, after an interval of four to nineteen weeks, were vaccinated again. Definite increases in the agglutination titer were noted following the second vaccination and when the vaccination was repeated from fifteen to twenty-eight weeks later, the titer rose again.

HANSEN, Minneapolis.

THE RECOVERY PERIOD IN ANTERIOR POLIOMYELITIS. N. M. HARRY, Brit. M. J. **1**:164 (Jan. 22) 1938.

Harry studied 36 patients with anterior poliomyelitis, keeping a careful graphic record of muscle response and voluntary muscle movement. He summarizes his conclusions as follows: 1. The period necessary for muscle reeducation is usually found to be much shorter than the period of spontaneous recovery. In the average case it is from nine to twelve months. 2. At from four to six months after the period of acute infection it is possible to determine the ultimate degree of recovery with fair accuracy.

He gives a brief outline of the methods of treatment and discusses the optimal time for treatment in recumbency. He makes a plea for the general adoption of graduated muscle charts as an aid both in treatment and in prognosis.

ROYSTER, University, Va.

DESIRABILITY OF COMPULSORY NOTIFICATION OF MEASLES AND WHOOPING COUGH. C. J. MCSWEENEY, Irish J. M. Sc., April 1938, p. 145.

This article is a discussion of the value of notification of health authorities of the occurrence of infectious disease.

SNELLING, Toronto, Canada.

A HISTORICAL, EPIDEMIOLOGICAL AND AETIOLOGICAL STUDY OF MEASLES (MORBILLI; RUBEOLA). J. A. H. BRINCKER, Proc. Roy. Soc. Med. **31**:807 (May) 1938.

Brinker opens his paper with a full definition of measles. In his historical survey of the disease he found that no descriptions of measles before the writings of Rhazes, in the tenth century, can be recognized. But Rhazes stated that he quoted from authorities who lived two hundred years before him. Measles was not accepted as an infectious disease until the sixteenth century. All through the early writings there was great confusion of measles with smallpox, but in 1629, in England, in the deaths returns the two diseases were entered separately. The word "measles" is of Teutonic origin, coming from a word *maes,* meaning a spot. "Morbilli" comes from the Italian *morbillo,* so-called to distinguish it from the plague which was known as *il morbo.* In 1808 Robert Watt made the earliest and most memorable analysis of cases in which children under 10 years of age died in Glasgow during thirty years. He pointed out that if child life is first attacked by smallpox and then by measles a lower fatality resulted than if measles occurred first. Therefore he thought that smallpox gave some immunity against measles. If smallpox preceded measles, however, it would kill delicate children and leave the strong ones, so that the fatality from measles would naturally be lower. This is true today, for, as the author points out when he discusses the incidence and mortality of measles, the fall in mortality has been due to improvements in child hygiene. He takes up in detail the geography, the etiology and the bacteriology of measles, the production of experimental measles, the characteristics of measles epidemics in Europe and America, the incidence and mortality, the periodicity of measles epidemics and the legal enactments. Lengthy tables and elaborate charts accompany the article, which illustrate the various points with which the writer deals.

WILLIAMSON, New Orleans.

ERUPTIVE FEVER OF OBSCURE ORIGIN. G. BLECHMANN and R. C. FRANÇOIS, Arch. de méd. d. enf. **41**:450 (July) 1938.

A case is reported in great detail to illustrate the difficulty of classifying certain eruptive diseases of childhood.

A girl of 5, in good health up to the age of 3, sustained during the fourth year a severe attack of polyarthritis, which subsided without cardiac involvement; several months later, having been taken to the tropics, she suffered an attack of amebic dysentery, for which sulfarsphenamine was employed. Following a relapse of this infection she was treated with acetarsone (stovarsol), 0.25 Gm. on four days each week for a month. A few weeks later the illness discussed in this contribution began, with fever, headache and angina. Under suitable treatment these symptoms disappeared promptly, only to recur on the sixth day, when a diffuse erythema, involving the cheeks and the entire trunk, appeared, and the picture resembled dengue fever. A consultant, however, felt that measles could not be excluded. The rash disappeared in two days; there was an interval of calm for forty-eight hours, and then the entire syndrome returned. At this time,

the rash was particularly confusing; it was general, with areas resembling the eruption of scarlatina and others simulating rubeola, while on the limbs a papular rash suggested a polymorphic erythema. There was intense conjunctivitis, a rather indefinite Koplik spot, mild angina and generalized intumescence of the lymph glands, especially of those in the inguinal and cervical regions. The chest disclosed no change. In view of the considerable amount of arsenic the child had received, a diagnosis of rubeola with toxic erythroderma was made, and intramuscular injections of magnesium hyposulfite were offered. There was immediate response, and in a few days complete recovery was observed. AMESSE, Denver.

CEREBROMENINGEAL EDEMA AND EPILEPSY IN CHICKENPOX. T. ALAJOUANINE, R. MARQUEZY, T. HORNET and LADET, Rev. neurol. **69**:76 (Jan.) 1938.

The authors report the occurrence of marked cerebral edema in a child in the course of a mild attack of chickenpox. Jacksonian convulsions, high fever and coma appeared, and within five hours the child was dead. The observations made at autopsy are given in detail. DAFFINEE, Boston.

CARRIERS AND THE EPIDEMIOLOGIC FACTORS IN ACUTE ANTERIOR POLIOMYELITIS. A. ROMANO, Riv. di clin. pediat. **36**:481 (June) 1938.

An epidemiologic study has been made on 200 cases of poliomyelitis that occurred during a period of ten years in the provinces of La Spezia, Lucca and Pistoia in Italy. The largest number of cases occurred in June and July and the next largest number in August and September. The most susceptible age group was that under 1 year. It was practically impossible to trace the contagion from one clinical case to another. There was no evidence that altitude, geographic location, insects, water or food were factors in the spread of the disease. Persons with undiagnosed poliomyelitis and carriers were probably responsible. The main prophylaxis against poliomyelitis should be the preventing of diffusion of the disease by contacts. HIGGINS, Boston.

INFLUENCE OF DIPHTHERITIC TOXIN ON THE BIOCHEMICAL STATE OF THE BLOOD. G. C. ABBA, Riv. di clin. pediat. **36**:714 (Aug.) 1938.

The chemical composition of the blood of guinea pigs was studied before and after they were given diphtheria toxin (¼ to 1 minimal lethal dose). There was a tendency for the sugar, cholesterol and calcium in the blood to fall and for the potassium and phosphate to rise as a result of the injections of the antitoxin. The changes were accompanied by signs of vagotonia. HIGGINS, Boston.

USE OF PLACENTAL EXTRACT IN THE CONTROL OF MEASLES. E. DIAZ MONTES, Rev. mex. de puericultura **8**:103 (Jan.) 1938.

Among infectious diseases, measles is one of the main causes of death in Mexico. Over the past ten years it has caused more than 10,000 deaths per year, an average of about 65 deaths per hundred thousand of population. Eighty-two per cent of the deaths occurred in children under 5 years of age. The author reports the use of placental extract in 600 children, 40 with measles and 560 contacts. Of 383 contacts followed, 289, or 75.46 per cent, were entirely protected; in 13.58 per cent the disease was modified greatly, and in 9.92 per cent it was attenuated to some degree, and in only 1.04 per cent was the use of the extract without effect. In 2.97 per cent there was a local reaction; in 24 per cent there was a febrile reaction; in 26.49 per cent both a local and a febrile reaction occurred; in 46.49 per cent no reaction was noted. In 77 per cent of those with fever the temperature was 100 F. or lower.

Naturally, the results depend on how early the extract is given to the contacts and on the amount used for intramuscular injection. HERRON, Monroe, La.

EXPERIENCES WITH PLACENTAL EXTRACT IN THE PROPHYLAXIS OF MEASLES. L. FREY, Med. Klin. **34**:218 (Feb. 18) 1938.

An intramuscular injection of from 10 to 25 cc. of placental extract between the first and fourth day of the period of incubation protected from 75 to 80 per cent of 47 children. Absolute protection in a high percentage of cases depends on large doses and injection early in the incubation period. Of 23 children given the extract between the first and third day of incubation, 91 per cent were protected. Early administration is rendered difficult by the fact that by the time of the appearance of the rash, four days of incubation has passed. With a single exception the 9 children in whom measles developed in spite of the protective inoculation were mildly affected.

Most of the children began to have pain at the site of injection from twelve to twenty-four hours later, which disappeared in about twelve hours. In a few moderate swelling occurred.

SIEMSEN, Chicago.

KOPLIK SPOTS IN EXUDATIVE DIATHESIS. I. H. ALANTAR, Monatschr. f. Kinderh. **73**:297 (June) 1938.

In an epidemic of measles Alantar noticed that certain of the children had a profusion of Koplik spots. In 3 children the spots were so numerous as to resemble thrush. He believes that those children showing the excessive number of Koplik spots were of the exudative type.

GERSTLEY, Chicago.

RECURRENCES OF WHOOPING COUGH. H. ZISCHINSKY, Wien. klin. Wchnschr. **51**:584 (May 27) 1938.

Zischinsky outlines 3 instances of a child being hospitalized for whooping cough three times. The intervals were about one year for one patient, one-half year for the second and about three months for the third.

In patient 2 the second and third attacks of pertussis were severe, with pulmonary complications. Identical pulmonary observations showed the relationship between the three attacks.

In patient 3 the second attack showed no signs of true pertussis except the cough. It was brought on by measles, and the cough was later attributed to a psychogenic reaction of the child, who had learned from his previous illness how to "whoop."

In most cases, however, recurrent whooping has an anatomic basis. Sometimes a new infection may be the cause, especially when the attacks are one, two or three years apart, but in the majority of cases the recurrence is due to the previous infection. Whenever the same lung changes are found, they almost certainly point to a flaring up of the old pertussis. Furthermore, the noncontagious nature of most of these later attacks indicate a residual, rather than a fresh, infection.

The onset of second and third attacks is frequently more sudden than that of the original one; often the catarrhal stage is lacking. Sometimes there are no warning symptoms. However, any infection of the upper air passages in a child who has previously had whooping cough may lead to a recurrence. These infections include grip, croup, measles and even the common cold.

ABT, Chicago.

EFFECT OF AN EXTRACT OF ADRENAL CORTEX IN MALIGNANT DIPHTHERIA. A. DOSKOCIL, Časop. lék. česk. **75**:606 (May 15) 1936.

Involvement of the adrenal cortex in malignant diphtheria led to the use of an extract of adrenal cortex as an adjuvant. Doskocil reports 24 cases in which the extract was used and gives a short review of the literature. The death rate in this series was 25 per cent in spite of the fact that several of the children did

not receive treatment until the end of the first week of the disease. Doskocil considers 5 cc. the smallest useful dose, and in very severe cases he recommends 10 cc. It is best to begin treatment early and to repeat the intravenous injection in from five to six days. There is no local action on the course of the disease, nor is there any action on the cardiac circulation. There is no effect on nerve palsies. In cases in which the disease has progressed to the point of massive engorgement of the liver there is no effect of treatment. STULIK, Chicago.

RELATION OF DIPHTHERITIC IMMUNITY TO GENERAL PHYSICAL DEVELOPMENT. J. VEJNAR, Časop. lék. česk. **75**:773 (June 19) 1936.

Vejnar examined 271 school children who were not immunized against diphtheria and who did not have clinical diphtheria. He divided these into five groups. The percentages of the positive reactions in the five groups were as follows: (1) well developed and well nourished children, 80; (2) average children (weight for height), 68; (3) children moderately below par, 61.9; (4) asthenic children, 64.8; (5) very asthenic children (asthenia gravis, etc.), 83.3. The difference is appreciable but not remarkable. STULIK, Chicago.

LATE POSTDIPHTHERITIC PALSIES. A. DOSKOCIL, Časop. lék. česk. **75**:912 (July 17) 1936.

Late postdiphtheritic palsies are important from the standpoint of rapid onset and localization and possible involvement of the bulbar centers. The etiologic factor is most likely the diphtheria toxin released from combination and modification of the antitoxin. Antitoxin is recommended to prevent any spreading of paralysis, even though it is felt that there is no effect on the already combined toxin and nerve tissue. STULIK, Chicago.

Acute Infectious Diseases

RABIES: REPORT OF TWELVE CASES, WITH A DISCUSSION OF PROPHYLAXIS. M. L. BLATT, S. J. HOFFMAN and M. SCHNEIDER, J. A. M. A. **111**:688 (Aug. 20) 1938.

In the eight years preceding 1937 there were admitted to the Cook County Hospital 12 patients with rabies. Their records are briefly incorporated in this article, as are photographs of the patients to illustrate some characteristic appearances. None of these patients received the recommended treatment for rabies, although 3 had injections of vaccine one week or more after they had been bitten. The public health aspects of the control of dogs and adequate care of all bites are emphasized. HEERSMA, Kalamazoo, Mich.

IMMUNOLOGIC REACTIONS FOR UNDULANT FEVER IN APPARENTLY HEALTHY AND IN TUBERCULOUS CHILDREN. J. R. LEWIN and I. GERSH, J. Pediat. **12**:571 (May) 1938.

It is recognized that, in spite of the fact that milk constitutes a larger factor in the diet of children than it does in that of adults, the incidence of clinical undulant fever in the former is less. The authors tested 310 children for evidence of past or present infection. In the first group of 222 children 170 were apparently healthy and 52 were in an institution for patients with tuberculosis, either because of active disease or because of malnutrition associated with definite or probable exposure to infection. The second group, 88 children, were seen in the outpatient department of the Colorado General Hospital. The first group were examined for evidence of an immunologic response to undulant fever by means of agglutination and intradermal tests. The results revealed that the incidence of intradermal immunologic reactions in the series of apparently healthy children was 3.53 per

cent, which was considerably less than the incidence encountered in adults, and that the occurrence of positive reactions was greater in the children confined in the preventorium than in apparently healthy children and that the incidence was greater in the children with active tuberculosis than in children confined to the preventorium. All the children who showed positive intradermal reactions gave a history of ingestion of raw milk. However, 107 of the 222 children (48.2 per cent) gave definite histories of having drunk raw milk and yet showed no immunologic response for undulant fever. This suggests that the susceptibility of the patient and perhaps the number of infecting organisms and the frequency of infection play a major role in the development of undulant fever. The 88 children attending the outpatient department were submitted to both the Mantoux test and an intradermal test for Brucella melitensis. There was a higher incidence of positive immunologic reactions among children showing a positive reaction to the Mantoux test than among children showing a negative reaction. This suggests either that raw milk is a common source of undulant fever as well as of tuberculosis or that tuberculosis renders the individual child less resistant to infection by B. melitensis.

RAUH, Cincinnati.

SIGNIFICANCE OF SHIGELLA ALKALESCENS (ANDREWES): A CLINICAL APPRAISAL OF NINE CASES FROM WHICH THE ORGANISM WAS ISOLATED. P. V. WOOLLEY JR. and M. SWEET, J. Pediat. **12**:596 (May) 1938.

Nine cases are reported in which infection with Shigella alkalescens was found. In 4 of these cases the organism was found in the urinary tract during an attack of pyelonephritis. In the remaining cases the organism was cultured from the stools during an attack of enteric infection. The bacteriology of S. alkalescens and its identification are discussed, and a brief review of the literature is presented.

RAUH, Cincinnati.

JUVENILE RHEUMATISM: THE THERAPEUTIC ASPECT. W. SHELDON, Lancet **1**:767 (April 2) 1938.

In juvenile rheumatism Sheldon includes three clinical conditions: (1) acute rheumatic arthritis; (2) rheumatic heart disease, including such occasional complications as rheumatic pneumonia, subcutaneous nodules and erythema marginatum; (3) rheumatic chorea. A fourth group, sometimes spoken of as subacute rheumatism, which includes vague aches and pains in muscles and joints, associated with anemia, irritability and fatigue, should not be included with the first three, as these pains, Sheldon feels, are no more than the accompaniments of a condition of debility that may come about from any one of a great variety of causes.

During the acute stage of rheumatism rest in bed remains the physician's sheet anchor; a month in bed should be the minimum. If the heart is affected, the rest should be longer. A sustaining diet, with an adequate supply of vitamins, is indicated.

Salicylate combined with alkali should be used energetically for rheumatic arthritis and in smaller doses may be used for the relief of pain in carditis, although in this condition a curative effect is not to be expected.

The author's experience with sulfanilamide in the treatment of rheumatism has so far been disappointing. Antistreptococcic serums and vaccines have also been of no avail.

As to prevention, Sheldon feels that from 20 to 30 grains (1.3 to 2 Gm.) of acetylsalicylic acid given daily throughout the one to four week interval between an acute infection of the upper part of the respiratory tract and the subsequent appearance of rheumatism may prevent or at any rate mitigate the rheumatic attack. He adds that it may be wise to treat similarly a child already rheumatic who has a sore throat, but that it is not practical to extend this principle to every child who has had an acute infection of the throat.

Early diagnosis of rheumatic heart disease, combined with prompt treatment and prolonged supervision, makes for a much improved prognosis.

LANGMANN, New York.

CHEMOTHERAPY OF PNEUMOCOCCAL AND OTHER INFECTIONS WITH 2-(P-AMINOBENZENESULPHONAMIDO) PYRIDINE. L. E. H. WHITBY, Lancet **1**:1210 (May 28) 1938.

The compound considered, 2-(paraaminobenzenesulfonamido)-pyridine, differs from sulfanilamide in that one hydrogen of the SO_2 NH_2 group is replaced by a basic pyridine group. It was found in experimental pneumococcic infections in mice that this drug was chemotherapeutically active against pneumococci of types I, II, III, V, VII and VIII, especially types I, VII and VIII. It appears to exert a definite action on the capsule of the pneumococcus. It is as active as sulfanilamide against the hemolytic streptococcus and the meningococcus, and it has a low toxicity for animals.

LANGMANN, New York.

DYSENTERY IN MEXICO CITY. A. CASTRREJON, Rev. mex. de puericultura **8**:187 (March) 1938.

In 51 per cent of 100 cases of dysentery the cause was traced to various types of the dysentery bacillus; in 30 per cent, to Endamoeba histolytica and in the rest, to mixed infections. The bacillary dysenteries were most prevalent from June to the last of August.

HERRON, Monroe, La.

TWO CASES OF TRICHINOSIS. S. GRACOSKI, V. NITZULESCU and C. HURMUZACHE, Bull. Soc. de pédiat. de Iasi **8**:5 (Jan.-June) 1937.

The authors report 2 cases of trichinosis occurring in children. The principal symptoms were fever, edema of the face and muscular pain. Both children showed marked eosinophilia, and when biopsy was done the encysted forms of trichinae were found in the muscle.

LESLIE, Evanston, Ill.

Chronic Infectious Diseases

CONGENITAL SYPHILIS (ANALYSIS OF THE PROBLEM IN MINNESOTA). F. W. LYNCH, Minnesota Med. **21**:313 (May) 1938.

Lynch feels that the present interest in the prevention and control of syphilis should be accompanied by increased attention to congenital syphilis, because this is a phase entirely controllable by prophylactic measures. He cites examples of professional failure and of the lax attitude of the public in the matter of cooperation and feels that education without control is not sufficient. In summarizing, he gives practical suggestions for the prevention of congenital syphilis and also states that if proper educational and medical procedures were followed, the congenital form of syphilis could be practically eliminated.

ANDERSON, Minneapolis.

COD LIVER OIL THERAPY IN EXPERIMENTAL TUBERCULOSIS. H. R. GETZ, Proc. Soc. Exper. Biol. & Med. **38**:543 (May) 1938.

Tuberculous ulcers of the skin were produced in guinea pigs by intracutaneous injections of 0.2 mg. of virulent tubercle bacilli, and they were then treated topically twice daily with a few drops of cod liver oil. The effective factor in healing these lesions was present in the unsaponifiable fractions but was not vitamin A or vitamin D, as was shown by work on 1,400 animals in eight series of experiments.

HANSEN, Minneapolis.

A Comparative Review of the Use of Antiluetic Drugs in the Treatment of Congenital Syphilis in Children. J. Yampolsky, South. M. J. **31**: 406 (April) 1938.

Yampolsky outlines the treatments which he uses for the various stages of congenital syphilis: For early congenital syphilis he advises (1) alternating treatment with preparations of arsenic and preparations of mercury or bismuth, injected intramuscularly, weekly or treating with each type of medicament for longer periods; (2) alternating the administration of acetarsone with injections of a preparation of bismuth. For late congenital syphilis he gives seventy-five injections of a preparation of bismuth and seventy-five full weeks' use of acetarsone.

Schlutz, Chicago.

Roentgen Picture of Pulmonary Tuberculosis in Children: Perihilar and Lobar Shadows. A. Piergrossi, Radiol. med. **24**:1007 (Dec.) 1937.

Dr. Piergrossi describes two roentgenographic phases of tuberculous pulmonary infections in infants: the triangular perihilar shadow, which has its base in the region of the hilus, and the lobar shadow, which occupies the major part or even the whole of one lobe. The shadows in question are due to different conditions, which can be distinguished by roentgen examination in the lateral view or with the aid of other signs. Either the perihilar shadow or the lobar shadow can rise (1) from epituberculous pulmonary infiltration, primary or secondary, in which case the perihilar shadow often represents a stage of evolution of the lobar shadow, (2) from developing pulmonary infiltration, either in the form of the primary phthisis of infancy or in the form of phthisic infiltration, both of which almost always give lobar shadows, or (3) from interlobar effusions. Among these Dr. Piergrossi distinguishes the primary effusions caused by a primary focus around an interlobar septum, which are hardly or not at all recognizable on roentgen examination, and the secondary effusions caused by hilar lymph glands, of which the diagnosis is easy.

In addition, the perihilar shadows can be connected with nonspecific perihilar lesions or even with specific or nonspecific lesions situated in front of or behind the hilus. However, Dr. Piergrossi estimates that it is hardly possible plainly to distinguish these last from the true perihilar forms, contrary to the opinion of certain authors.

Martoccio, Utica, N. Y.

Treatment of Congenital Syphilis. A. Navarro H., Rev. mex. de puericultura **7**:535 (Oct.) 1937.

The treatment of congenital syphilis has been given much study and has been the subject of many interesting experiments. Navarro still believes that mercury inunctions are of great value. He discusses in detail the use of each of the following drugs in their variable compounds: mercury, arsenic, bismuth and the iodides. He likes to use acetarsone (stovarsol). He suggests that no one drug should be used for any patient, but a combination of drugs. This article is an excellent review of the various drugs, the doses and the various methods of use, and the subject matter is well presented.

Herron, Monroe, La.

Infantile Tuberculosis. H. L. Castaneda, Rev. mex. de puericultura **8**:3 (Nov.) 1937.

Under tuberculosis Castaneda discusses the bacillus, heredity, contacts, views about the mode of entrance of the organism into the body of the infant, the cutaneous reactions to tuberculin, the roentgen examination, the physical examination and findings, the classification of infantile tuberculosis as to types, prophylactic treatment and other methods of treatment. In general, he gives a good résumé of the subject.

Herron, Monroe, La.

SOME ANATOMIC-PATHOLOGIC CHARACTERISTICS OF CHILDHOOD PULMONARY TUBERCULOSIS. A. Vergara E., Rev. mex. de puericultura **8**:28 (Nov.) 1937.

Vergara discusses in detail the common pathologic aspects of the various types of childhood pulmonary tuberculosis. HERRON, Monroe, La.

THREE CASES OF INFANTILE TUBERCULOSIS. P. RUEDA, Rev. Soc. de pediat. de Rosario **3**:8 (March) 1938.

The first case was one of confluent cutaneous papular areas about the face and back in a child of 2 years. Roentgenograms showed the lungs to be involved. The second case was observed in a child of 10 years. The primary lesion was an old scar in the popliteal area, with necrosis of the glands in Scarpa's triangle. Roentgenograms of the lungs showed no involvement. A report of the third case will be published later in this journal. SANFORD, Chicago.

EVALUATION OF ROENTGEN FINDINGS IN CHILDHOOD TUBERCULOSIS. O. CHIARI, Wien. klin. Wchnschr. **51**:414 (April 8) 1938.

Chiari, of Vienna, observes that often one finds the roentgenogram negative in spite of the fact that tuberculosis is active, especially in cases of new primary infection. On the other hand, the physician should realize that spots and striae in the region of the hilus may occur in nontuberculous children. An increase in the size of shadows at the hili may be observed in nonspecific diseases. In particular, chronic or residual bronchopneumonia affects the paramediastinal parts of both lungs.

Marked shadow formation in the hilar region with less sharp boundaries toward the field of the lungs is characteristic of tuberculosis. One finds the so-called perihilar infiltrate especially noticeable in new tuberculosis; however, a centrally beginning pneumonia can cause a similar picture, so the clinical findings must determine the differential diagnosis.

Especially characteristic of tuberculosis is the stage of bipolarity. A round localized shadow in the lungs is joined by a small pedicle to the shadow in the region of the hilus. This same finding may also be observed at the beginning of pneumonia. Extensive homogeneous shadowing in the lungs may indicate so-called infiltration from the primary focus but may also represent caseous pneumonia, especially if the patient is a child. Transparent foci in the shadows do not necessarily indicate cavity formation in caseous pneumonia, since pseudocavities which arise in air-containing emphysematous tissues in the midst of other tissues which have thickened, also occur through the solution of specific and unspecific infiltrates.

Likewise abscesses of the lungs must be taken into consideration in the differential diagnosis. Even miliary tuberculosis may be confused with miliary pneumonia. Deposits of lime in the lungs are probable evidence of a tuberculous process; they indicate that the illness began a considerable time previously but do not exclude the possibility that it is still active owing to the fact that the process may progress beyond the healed parts to other tissue. This is especially true in tuberculosis of the bronchial glands. However, such calcification in a child reacting to tuberculin should be considered a negative finding.

These early forms of tuberculosis are almost all benign if one excludes the miliary type of the disease. Their recognition postulates no immediate special measures, since their infectiousness is slight; a general strengthening treatment, with plenty of fresh air, is needed.

The phthisis of puberty, however, is different. Here the roentgen finding is of special value, since it alone makes early diagnosis possible. The discovery of an early infiltrate, indicating disintegration, is the occasion for immediate action. Pneumothorax is indicated so long as no certain cavities are observed. Any slight disturbance in the general well-being of the child who has a hereditary taint calls for roentgenography. The clinical finding is often negative, even though

bacilli can be seen in the sputum. A negative roentgen finding should be checked again in four weeks if the clinical symptoms persist.

In tuberculosis of the skeleton roentgen study is especially important. An early diagnosis of spondylitis or coxitis is unlikely. Negative findings in the presence of clinical suspicions are not always reliable; usually the roentgen picture follows the clinical findings by about one week.

It should be noted that even in childhood the roentgenographic differential diagnosis between tuberculosis and other skeletal diseases is difficult. It is especially hard to distinguish between osteochondritis and tuberculous coxitis, but every effort should be made and the exacting regimen for coxitis should not be adopted without roentgenographic evidence. In doubtful cases the hip joint should undergo a rest until the diagnosis becomes clear.

Only the consideration of all clinical symptoms with the roentgen findings can lead to proper evaluation of the picture of the disease and show the way to correct treatment.

ABT, Chicago.

EXPERIENCES IN THE TREATMENT OF PATIENTS FOR UNILATERAL PULMONARY TUBERCULOSIS. P. J. L. DE BLOEME, Nederl. tijdschr. v. geneesk. **82**:1309 (March 19) 1938.

Bloeme concludes from his experiences in the treatment of 1,260 patients during a period of five years that no special treatment is necessary if the positive sputum becomes free from bacilli after from two to three months of adequate rest in bed. The majority of patients whose lungs contain cavities (e. g. 71 per cent) require collapse therapy. Monthly examinations of the sputum indicate how long observation without collapse therapy is advisable. If the sputum is not free from bacilli after from two to three months, intervention is necessary. In this manner nature's ways are imitated. The total duration of the treatment can be reduced to that of the natural treatment. The total duration of the treatment averages between twelve and fifteen months, during which time the sputum remains free from bacilli on an average of nine months. Complete working capacity is restored to 80 per cent of the patients. Between 70 and 80 per cent of the patients lose the bacilli before discharge from the sanatorium. Unilateral pulmonary tuberculosis with sputum containing bacilli requires treatment in a sanatorium. Noninstitutional treatment is not justified in the majority of cases.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Blood, Heart and Blood Vessels and Spleen

INCIDENCE AND TYPE OF HEART DISEASE IN SAN FRANCISCO SCHOOL CHILDREN. J. J. SAMPSON, A. CHRISTIE and J. C. GEIGER, Am. Heart J. **15**:661 (June) 1938.

In a number of studies on San Francisco school children, the percentage of children with congenital heart disease in the group with organic heart disease was found to be extremely high, from which fact it was concluded that the incidence of rheumatic heart disease was correspondingly low.

A sample of 13,338 school children included 197 children suspected of having heart disease. In this group the incidence of organic heart disease per thousand of population was 3.7; of rheumatic heart disease, 2.2; of congenital heart disease, 1.4.

GIBSON, Chicago.

COARCTATION OF THE AORTA AT AN UNUSUAL SITE, ASSOCIATED WITH A CONGENITALLY BICUSPID AORTIC VALVE. R. L. PARKER and T. J. DRY, Am. Heart J. **15**:739 (June) 1938.

A case of coarctation of the aorta is reported in which the site of stenosis was between the left common carotid and left subclavian arteries. The blood pressure

in the right arm was 210 systolic and 40 diastolic, and that in the left arm, 100 systolic and 78 diastolic. In the arteries of the lower extremities no pulsation could be felt. No evidence of collateral circulation could be obtained. A congenitally bicuspid aortic valve was the seat of subacute vegetative endocarditis.

GIBSON, Chicago.

EFFECT OF PRONTOSIL AND RELATED COMPOUNDS UPON THE CHEMOTROPISM OF LEUKOCYTES. D. R. COMAN, Am. J. M. Sc. **196**:273 (Aug.) 1938.

Coman conducted experiments using prontosil (the disodium salt of 4-sulfamidophenyl-2′-azo-7′- acetylamino - 1′- hydroxynaphthalene - 3′, 6′- disulfonic acid) adsorbed on kaolin, carbon and streptococci in an attempt to determine the chemotropic effect of the drug on polymorphonuclear leukocytes. Leukocytes were obtained from the peritoneal cavity of the rabbit. This drug slightly reduced the negative chemotropic effect of kaolin. Adsorbed to carbon and to streptococci, it did not alter the directional movement of the leukocytes in relation to the adsorbing agents.

Experiments in which sulfanilamide was used as the attracting substance showed that in the concentrations used this substance exerted a toxic effect on the leukocytes, which was expressed in cessation of their movements. Coman concludes that the therapeutic action of these drugs is probably due to the fact that they increased chemotropism for polymorphonuclear leukocytes.

ENSKE.

HEART DISEASE IN CHILDHOOD. T. D. JONES, Am. J. Pub. Health **28**:637 (May) 1938.

The author gives the results of a ten year follow-up of 1,000 patients with rheumatic fever treated at the House of the Good Samaritan, Boston. Of these 1,000 children, 242 (24.2 per cent) are dead, 310 are potential subjects of rheumatic heart disease, and 427 have rheumatic heart disease. On 21, the data are insufficient. Of the 427 living patients with rheumatic heart disease, there is no limitation of activity in 287, the limitation is moderate in 119, and in 21 there is a serious physical handicap.

Until more is known regarding the disease, measures for control consist (1) in early recognition of the disease and (2) in prevention of respiratory infections in rheumatic subjects.

LIMPER, Louisville, Ky.

ANEMIAS IN DIGESTIVE DISEASES OF CHILDREN. I. N. KUGELMASS, Arch. Pediat. **55**:268 (May) 1938.

The generation of new blood cells is dependent not only on a sufficient supply of specific food elements but also on a large number of nonspecific nutrients that are necessary for maintenance of the body as a whole.

Nutritional requirements should not be considered in terms of amounts of protein, carbohydrates, fats, minerals and vitamins but in terms of optional amounts of: twenty-two amino acids from protein; dextrose from carbohydrate; linoleic acid from unsaturated fats; twelve minerals from fruits and vegetables; ten vitamins from various types of foods; water, and oxygen. The formation of blood cells by the reticuloendothelial system necessitates special nutritional factors, such as: arginine, glutamic acid, protein and oxyprotein from protein; iron, copper, manganese, nickel and other minerals; the extrinsic factor of liver and other viscera, and vitamins B_2, C and D.

ORR, Buffalo.

COARCTATION OF THE AORTA WITH UNEQUAL BLOOD PRESSURE IN THE ARMS: A CASE REPORT. R. G. HILLS, Bull. Johns Hopkins Hosp. **62**:475 (May) 1938.

The blood pressure in the right arm was 180 systolic and 100 diastolic, that in the left arm 110 systolic and 85 diastolic, and that in the legs 110 systolic and 90 diastolic. Roentgen examination showed the arch of the aorta to be increased in width, but the ascending portion of the arch could not be clearly visualized under the fluoroscope. The ribs showed moderate notching of the type seen in patients with coarctation of the aorta. The author notes that anatomic narrowing of the left subclavian artery has been reported in association with coarctation of the aorta and assumes that this explains the normal blood pressure in the left arm and the hypertension in the right arm.

LYTTLE, New York.

STUDIES CONCERNING HYPERTENSION IN CHILDHOOD: I. THE DEVELOPMENT OF ESSENTIAL HYPERTENSION UNDER OBSERVATION. H. B. TAUSSIG and M. S. HECHT, Bull. Johns Hopkins Hosp. **62**:482 (May) 1938.

Three cases are reported in which during the course of a rheumatic infection hypertension developed under observation.

The importance of abnormally high blood pressure in young children is emphasized.

FROM AUTHORS' SUMMARY.

STUDIES CONCERNING HYPERTENSION IN CHILDHOOD: II. THE OCCURRENCE OF HYPERTENSION IN ACUTE RHEUMATIC FEVER IN CHILDHOOD. H. B. TAUSSIG and M. S. HECHT, Bull. Johns Hopkins Hosp. **62**:491 (May) 1938.

Thirty-seven cases are reported in which hypertension occurred in close connection with an acute rheumatic episode—chorea, chorea and rheumatic fever, or rheumatic fever.

Twelve additional cases are reported in which high blood pressure has been recorded over a long period of time and in which the blood pressure still fluctuates widely. The patients have not been followed for a sufficient length of time to determine whether the hypertension will become permanent.

The various conditions under which hypertension has been observed are analyzed. Hypertension was not associated with demonstrable renal damage. Its frequent association with some manifestation of rheumatic activity strongly suggests that it is related to active rheumatic infection. The exact relation between hypertension and rheumatic infection is not clear. Various possibilities are discussed.

FROM AUTHORS' SUMMARY.

REVIEW OF A CASE OF THROMBO-CYTOPENIC PURPURA TREATED BY SPLENECTOMY. G. T. AITKEN, J. Michigan M. Soc. **37**:628 (July) 1938.

Aitken reviews the case of a 6 year old boy who was admitted to the hospital in 1931 for compound fracture of the right tibia and fibula complicated by osteomyelitis. The end results of treatment were satisfactory. On one of the boy's return visits to the hospital, it was necessary to admit him because of frequent and severe nosebleeds. Later he was admitted because of a severe sore throat. He had several hemorrhages from the nasal mucous membrane which necessitated transfusions. The diagnosis made at this time was thrombopenic purpura. A study of the blood made three months later gave a diagnosis of aplastic anemia. Supportive treatments were used, including blood transfusion and injection of pigeon serum and snake venom, but hemorrhages from mucous membranes and into subcutaneous tissues continued.

After months of repeated treatments, splenectomy was performed. The recovery was uneventful, and a year later, it is reported, "a chronic invalid became a normal individual."

CAREY, Detroit.

ERYTHROBLASTOSES OF INFANCY. M. PÉHU and R. NOEL, Arch. de méd. d. enf. **41**:321 (June) 1938.

During the past twenty-five years the attention of the clinician and the hematologist has been attracted increasingly to a group of diseases or syndromes commonly associated with the occurrence of large numbers of nucleated red cells in the peripheral blood and in certain organs not normally concerned with hemopoiesis; in addition, these diseases are often characterized by tumefaction of the spleen and liver, increase in bilirubin in the blood serum and urobilinuria. The importance attached to these unusual features brings up several pertinent questions. What is the pathologic significance of a condition in which normal blood corpuscles are found accompanied by immature, imperfectly developed, nucleated forms? Should erythroblastosis be recognized as a definite entity in pathology?

The histology of the normal corpuscle is fully discussed in this extensive monograph, and a complete historical review is made of the erythroblastoses from their earliest description, by Hermann Rautmann, in 1912.

The terminology of these obscure diseases of early life is accorded unusual attention, since certain expressions, frequently employed in the growing literature, are apt to be confusing.

An analytic study divides them into (*a*) symptomatic, secondary complexes and (*b*) primary erythroblastoses. The thesis concludes with a comprehensive nosologic schema and a complete bibliography.

AMESSE, Denver.

FAMILIAL VON JAKSCH-LUZET ANEMIA OF THE COOLEY TYPE. A. SANTILLANA, Arch. de méd. d. enf. **41**:356 (June) 1938.

Pseudoleukemic anemia of nurslings, of unknown cause, is characterized clinically by extreme pallor, splenomegaly of variable degree, cachexia, more or less pronounced, and rachitic deformities. Luzet stated that the blood showed definite changes, such as diminution in the density of both hemoglobin and corpuscles, progressive increase in the number of leukocytes, changes in the morphologic character of the red cells and appearance of large numbers of erythroblasts.

After reviewing briefly the contributions by European and American investigators in this field, Santillana reports his observations on 4 children of a Sicilian family established in Tunis, Algeria. The parents were not of the same stock; they had never been ill, and their blood gave a negative Wassermann reaction. Santillana had observed the children since their birth. The youngest subject was 2 months of age, and the eldest, 6½ years. Of the 4 children, all but the eldest showed the typical features of von Jaksch-Luzet anemia; in addition, 2 of them, aged 17 months and 4 years, respectively, exhibited the pathognomonic signs of Cooley's disease in their mongoloid facies and in the osseous changes presented in complete roentgenologic studies. One child, a girl, continues in normal health at the age of 6½ years.

Such instances should stimulate further the study of the hereditary factors acting principally on the hemopoietic organs of the growing infant before birth and should furnish material for an inquiry on the relationship of the disease in question.

AMESSE, Denver.

A CONTRIBUTION TO THE STUDY OF THE TERRAIN IN HEMATOLOGY. G. MOURIQUAND, L. WEILL, V. EDEL and J. FERRI, Arch. de méd. d. enf. **41**:369 (June) 1938.

Not one acceptable hypothesis has been advanced to clarify the genesis of the primary anemias of the newborn. All of these anemias, however, have one characteristic in common; they supervene on a particular terrain. Some of them, e. g., the erythroblastoses of the newborn, are familial; others, e. g., hemolytic icterus, are at once familial and hereditary; one important member, Cooley's

disease, is racial and occurs only in subjects of Mediterranean origin. Heredity, however, does not constitute the whole of what is here designated as the terrain.

Parsons was able to produce anemia in female rats, and the progeny of these rats were frequently found to be anemic even after the maternal rats had recovered. Various other workers have investigated anemias resulting from a combination of factors incapable singly of producing marked hematologic disturbance; experimentally, the use of aminopyrine or indole in certain diseases of dogs, such as black tongue, will promptly produce anemia.

The authors demonstrated their theory by producing acute experimental anemia in scorbutic guinea pigs, in which nucleated red cells are rarely found: Pregnant females were first inoculated with the anatoxin of diphtheria (Ramon) and their young also inoculated, subcutaneously, at the age of 1 week; scurvy was then produced by an exclusive diet of barley and grass; the onset of the scurvy was signalized by the appearance of large numbers of normoblasts, and polynucleosis was replaced by mononucleosis.

AMESSE, Denver.

PRACTICAL TESTING OF CARDIAC CAPACITY FOR WORK IN THE CHILD. F. HAMBURGER, Med. Klin. **34**:391 (March 25) 1938.

In the final analysis, cardiac capacity for work is more important than any condition disclosed by physical, roentgen or electrocardiographic examination. Furthermore, the child as a physical and mental organism deserves consideration, as well as his heart. With patients in bed (without fever or involvement of joints) the activity used in testing can be rising to the sitting position several times; for ambulatory patients it can be squatting or stair climbing. The physician can accompany and observe a child on a walk (over a level surface or uphill). Acceleration of respiration and dyspnea are more important than acceleration of heart action, which may be affected by psychic influences. Respirations should be observed without the child's knowledge. Conversation or counting may reveal dyspnea.

SIEMSEN, Chicago.

COOLEY'S ANEMIA. A. PANOFF, Monatschr. f. Kinderh. **73**:184 (May) 1938.

Panoff reports 2 cases of Cooley's anemia. The report is of interest because it indicates that for the first time the disease has been studied in Bulgarian children. In discussing the causes and reviewing the literature to some extent, the author agrees with others that the condition is an inherited constitutional anemia. He disagrees with those who favor the idea that it has its origin in abnormal erythropoiesis. On the basis of examinations of marrow obtained by sternal punctures he believes that the pathologic condition is a diminished ability of the bone marrow to retain unripe nucleated red cells.

GERSTLEY, Chicago.

INFECTION AND BLOOD DESTRUCTION IN CHILDHOOD. F. THOENES, Monatschr. f. Kinderh. **73**:197 (May) 1938.

Thoenes does not believe that the acid-soluble iron in serum is there as a direct result of the consumption of iron but rather as a result of the disintegration of hemoglobin. Supporting this statement, he offers the argument that this acid-soluble iron is affected neither by diet nor by hunger, that it increases with processes which cause destruction of hemoglobin and that it decreases with anemia due to loss of blood. The present study was made to determine what effect infection has. The method was to determine the output of urobilin. The results show a considerable increase in urobilin in infections both with and without fever and in some cases fevers induced by chemical agents.

He concludes that not only severe infections but even milder ones cause increased destruction of blood and through increased demands on the regenerative strength of the bone marrow lead to postinfectious anemia.

GERSTLEY, Chicago.

A Source of Error in the White Blood Cell Count. J. Engelbreth-Holm and C. C. Winkel Smith, Acta med. Scandinav. **95**:129, 1938.

White blood cells in heparinized or citrated blood disintegrate fairly rapidly. Even in Türk's dilution fluid, in some cases, the white cell count may fall 10 to 20 per cent in from six to twenty-four hours' standing, while in other cases the white cells are stable.

If a cell count cannot be done immediately, it is recommended that a new dilution fluid be used (saponin, 0.2 Gm.; methyl violet, 0.1 Gm.; sodium fluoride, 2 Gm., and distilled water, 200 Gm.). This fluid preserves the white cells over twenty-four hours. Because of its fluoride content, it has to be kept in a paraffin-coated bottle.

Kajdi, Baltimore.

Acute Hemolytic Anemia (Lederer). J. Mendels, Nederl. tijdschr. v. geneesk. **82**:536 (Jan. 29) 1938.

Mendels records 4 cases of acute hemolytic anemia (Lederer). One of the patients was a member of a family in which another member had shown acholuric jaundice.

van Creveld, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

Prognosis in Cases of Tuberculosis of the Tonsils, Adenoids and Cervical Lymph Nodes: A Study of Patients Followed for Eleven to Twenty-Three Years. J. Bordley III and J. W. Baylor, Bull. Johns Hopkins Hosp. **63**:132 (Sept.) 1938.

Seventy-nine patients who at operation between 1912 and 1924 were discovered to have tuberculosis of the tonsils or adenoids were subjected to reinvestigation in 1935. Of 47 patients operated on prior to the age of 14 years, 45 could be traced; 2 of these had died of nontuberculous diseases, and 1, of tuberculous meningitis several months after operation. All the 42 living patients were well. The 2 patients who could not be traced were well when last seen, from fifteen to twenty-two months after operation. In this group the incidence of serious tuberculous sequelae was very low, and no patient showed any evidence of having acquired pulmonary tuberculosis of the adult type since the operation. The high incidence of tuberculous cervical adenitis and the complete absence of progressive pulmonary tuberculosis among these patients constitute an interesting observation in view of the controversy concerning the prognosis in this form of tuberculosis.

Lyttle, New York.

Paranasal Sinus Disease in Children. S. Z. Faier, Nebraska M. J. **23**:370 (Oct.) 1938.

It is reasonable to suppose that diseases of the nasal sinuses are not rare in children though often overlooked. Such factors as deficiencies in the diet, allergy and other abnormal conditions, such as local obstructions, are worthy of attention. The ethmoidal cells are always present at birth, and the maxillary sinuses are only rarely absent. The presence of swollen membranes about the ostium of a sinus, foreign bodies, tumors or anything else that causes stagnation always results in infection. Roentgen examination should be made early rather than late. If there is malnutrition, chronic arthritis, chronic bronchitis, bronchiectasis or other systemic infection, tonsillectomy and adenoidectomy often improve the child's general condition. Listlessness, poor appetite, underweight and anemia suggest the possibility of chronic sinus infection. In acute involvement of the sinuses the predominant symptoms are nasal stoppage or a feeling of fulness in the head with nasal discharge; pain and headache may be brought about by closed empyema. In older children a small mirror can be used for postnasal examination. Smears may

reveal either a large number of pus cells or a predominance of eosinophils, indicating allergy. Swelling of the eyelids and cheeks, tenderness of the involved sinus and enlargement of the postcervical glands are often present. Cooperation between the otolaryngologist and the pediatrician is necessary. In a greater percentage of the cases of sinus infection operation for the removal of obstructions is sufficient. The aim of treatment is to obtain ventilation and drainage by the simplest method possible. In a large percentage of cases, chronic sinus infection in a child clears up with removal of the tonsils and adenoids.

HAMILTON, Omaha.

A VOLUMINOUS CHONDROMA OF THE LEFT ETHMOID REGION WITH MUCOCELES IN ALL SINUSES AND A GRAVE OCULAR SYNDROME. E. RUBALTELLI, Riv. oto-neuro-oftal. **14**:48 (Jan.-Feb.) 1937.

A boy of 16 years who appeared to be in good health noted progressive divergence of the left eye, protrusion of the globe and marked reduction in vision. The disk was red and slightly elevated, with well defined edges and with markedly dilated and tortuous veins. Examination of the nose gave negative results. Palpation revealed a hard painless mass in the superomedial portion of the orbit. It was firmly fixed to the medial wall, from which it seemed to rise. Roentgenographically an opaque mass could be demonstrated occupying the ethmoid cells and extending into the nasal fossa, orbit and maxillary sinus of the same side. In addition, the frontal and maxillary sinuses were clouded.

The mass was removed by Citelli's transmaxillary and central facial approach. It had an osteocartilaginous consistency and microscopically showed the characteristics of a chondroma. In addition, two large mucoceles were found occupying the frontal and maxillary sinuses. Postoperative examination showed that vision, fundus and mobility had returned to normal. The text is illustrated with 9 photographs and drawings.

F. P. GUIDA. [ARCH. OPHTH.]

FOREIGN BODIES IN THE RESPIRATORY TRACT. T. FALCÃO, An. de oto-rino-laring. **3**:106 (June) 1937.

Falcão has removed foreign bodies from the upper segments of the respiratory tract in 22 cases. In 10 of the cases the body was removed by means of a pincet introduced through a bronchoscope under roentgen visualization. The diagnosis is made by roentgen examination of the neck and bronchial region. For removal of a foreign body from a bronchus, the patient is placed in the dorsal position before the roentgen screen; the head is turned to the side involved; the bronchus is anesthetized through the bronchoscope, which can be introduced by the mouth, and the foreign body, under the roentgen control, is grasped with a pincet and easily removed.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TONSILS AND FOCAL INFECTION. A. MOURA, An. de oto-rino-laring. **3**:121 (June) 1937.

According to Moura, complete tonsils and remnants of those not completely removed are frequently the seat of focal infection, and such infection is suspected of having its origin in infected teeth. When the tonsil is infected, the symptoms intensify during tonsillitic crises and change after external massage on the tonsillar region. If such changes are noted, removal of the tonsils (or of the portions left after an imperfect tonsillectomy) induces recovery of the patient. Even if the symptoms are not clear, tonsillar infection may be present. Extraction of the teeth in cases of an uncertain diagnosis fails to bring about improvement in the patient's condition but succeeds in discounting the theory of focal infection, which has been exaggerated.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

A Study of the Prognosis and Complications of Otitis Media Based on Material from the Otolaryngologic Clinic of Professor Precechtel from 1923 Through 1932. E. Kertesz and Z. Kocka, Časop. lék. česk. **75**:433 (April 10); 496 (April 17); 513 (April 24) 1936.

The authors report on 23,301 cases of otitis media, which were 22.8 per cent of the total of 102,225 cases in which treatment was given in the otolaryngologic clinic. In 32.4 per cent of these the otitis was acute and in 67.6 per cent it was chronic. In 81 per cent of the cases of acute otitis media the ear drum was perforated, and in 19 per cent it was not. Complications were: mastoiditis, in 10.4 per cent of all cases of otitis; subperiosteal abscess, in 1.2 per cent; Bezold's abscess, in 0.27 per cent; subcranial abscess, in 0.07 per cent; other collar abscesses, in 0.17 per cent; temporal abscess, in 0.04 per cent, and postoperative scars, in 0.3 per cent. Retroauricular fistulas were found in 0.44 per cent of cases, labyrinthine fistulas in 0.35 per cent, diffuse suppurative labyrinthitis in 0.2 per cent and paralysis of the facial nerve in 1 per cent. Of the intracranial infections, 924, or 3.96 per cent, were dural; 121, or 0.51 per cent, were extradural and included the perisinusal. In 124, or 0.53 per cent, of the cases there was thrombophlebitis of the sigmoid sinus; in 94, or 0.40 per cent, otogenic meningitis; in 46, or 0.20 per cent, brain abscess (in 24 cerebral, in 20 cerebellar and in 2 combined); in 10, or 0.04 per cent, encephalitis, and in 8, or 0.03 per cent, subdural abscess. In 155, or 0.66 per cent of the cases, otogenic sepsis developed. One hundred and twenty, or 0.51 per cent of the patients, died of complications of otitis, and of these 53 had acute and 67 chronic forms. Fourteen other patients died of non-otitic complications. The cause of death was meningitis in 78 cases, thrombophlebitis in 60 cases and cerebral abscess in 28 cases, or a combination of one, two or three of these. Of the patients with suppurative otogenous meningitis, 16, or 16 per cent, recovered, and in the last, three years cures of meningitis have increased to 30.4 per cent. Recoveries from thrombophlebitis took place in 64, or 51.6 per cent of the cases; from cerebral abscess, in 18, or 39.1 per cent, and of the 34 patients treated surgically, 18, or 52.9 per cent, recovered, which is the highest percentage recorded in the literature. Of the patients with encephalitis, 4, or 40 per cent, and of the patients with the subdural abscesses, 2, or 25 per cent, recovered.

Stulik, Chicago.

Diseases of Lungs, Pleura and Mediastinum

Tracheo-Esophageal Fistula. H. A. Gamble, Ann. Surg. **107**:701 (May) 1938.

The congenital anomaly known as atresia of the esophagus with tracheo-esophageal fistula is comparatively infrequent but by no means as rare as it is usually considered. Rosenthal in 1931 compiled a list of 255 cases. Gamble has observed 2 cases within the past seven years. One of these cases he reports, together with a new operative procedure.

The treatment is essentially surgical. The surgical approach is either by a direct attack on the condition or by indirect procedure. In the indirect approach at least three stages are necessary. The objectives in the first stage are: (1) to provide a means of nourishing the child; (2) to prevent regurgitation of food; (3) to prevent pulmonary complications. The second stage is concerned with reconstruction of the esophagus, and the third stage has to do with reestablishment of the continuity of the gastrointestinal tract.

The operation which the author describes, despite its formidable appearance, is, he states, well tolerated by the infants and fulfils all the conditions postulated.

Bantin, Omaha.

A Simple Treatment for Empyema in Children. B. C. Willis, Ann. Surg. **107**:739 (May) 1938.

Willis bases his opinion on the study of 104 consecutive cases. He believes that the punch operation carries a lower mortality, if care is taken to keep the cavities clean and improve the child's general health. He gives his technic in detail. Blood transfusions in the course of the treatment are valuable. Also, emphasis is placed on such postoperative treatment as exercise of the chest, calisthenics and bottle blowing. Fresh air, regular rest, a generous diet, cod liver oil and vitamins should be prescribed.

Bantin, Omaha.

Pathogenesis of Bronchiectasis. F. P. L. Lander and M. Davidson, Brit. M. J. **1**:1047 (May 14) 1938.

The investigation reported was based on a hypothesis of the authors. Two cases are described: In one of these there was roentgenologic proof of the presence of bronchiectasis for a period of ten years; in the other there was strong presumptive evidence of pulmonary collapse of thirteen years' standing. Comparative bronchograms in these cases showed that the affected bronchi retained their full degree of elasticity despite their dilatation.

The persistence of normally functioning elastic tissue in bronchi thus distorted affords a strong argument against the theory that infection of the bronchial wall is the primary cause of bronchiectasis.

Royster, Charlottesville, Va.

Function of the Bronchial Tubes. M. Ellis, Lancet **1**:819 (April 9) 1938.

Ellis bases his article on experiments on the larger bronchi. The behavior of the smaller ones is deduced by analogy.

The bronchial muscle is concerned entirely with the maintenance of a moderate tone, and there seems to be no rapid rhythmic function assignable to it.

The larger bronchi are able to resist changes of shape, especially compression, imposed on them by the respiratory movements of the thorax because of the plaques of cartilage in their walls. In the unsupported smaller bronchi, the muscle forms a relatively larger proportion of the wall and by its tone prevents the expiratory movements from occluding the lumens of the tubes.

In spasmodic bronchial disease it is not necessary to postulate an active contraction of the bronchial muscle—a small increase in tone will produce far reaching effects. By stimulating with a faradic current an area on the left side of the nasal septum a prolonged bronchial constriction was caused, proving that the nasobronchial reflex is not a homolateral phenomenon as has been widely held, but is certainly contralateral and probably bilateral.

Langmann, New York.

Treatment of Pneumonia with 2-(p-Aminobenzenesulphonamido) Pyridine. G. M. Evans and W. F. Gaisford, Lancet **2**:14 (July 2) 1938.

The ages of the patients, both the treated ones and the controls, ranged from 8 to 68 years. The mortality in 100 patients with lobar pneumonia who were treated with the drug was 8 per cent as compared with 27 per cent in a control series observed at the same time.

At first the drug was given in smaller doses because of fear of granulopenia, but when no tendency in this direction was noted, it was decided to administer large doses during the seventy-two hours immediately following admission; 2 grains (0.13 Gm., i. e., 4 tablets) was given immediately and 1 grain (0.06 Gm.) at four hour intervals thereafter, making an average total intake of about 25 grains (1.6 Gm.). Cyanosis appeared in about 25 per cent of the intensively treated patients but disappeared promptly when the drug was withdrawn. Spectroscopic examination revealed methemoglobin in 6 cases.

In addition to the aforesaid series, patients in the children's wards suffering from pneumonia, bronchopneumonia, otitis and infection of the upper part of the respiratory tract were treated with the drug. Forty patients with bronchopneumonia were treated; of these, 2 died.

No difficulty was encountered in getting any of the babies to take the tablets, which were crushed and suspended in milk or dextrose-salt solution. No toxic manifestations were observed.

LANGMANN, New York.

PNEUMOCOCCIC EMPYEMA TREATED SUCCESSFULLY WITH PRONTOSIL BY MOUTH. S. GRACOSKI, C. MURMUZACHE and T. MARCULESCU, Bull. Soc. de pédiat. de Iasi **8**:15 (Jan.-June) 1937.

The authors present 3 cases in which a more rapid recovery from pneumococcic empyema occurred with the use of prontosil (a derivative of sulfanilamide). In all cases, however, the pus was aspirated, also.

LESLIE, Evanston, Ill.

CONGENITAL CYSTS OF THE LUNG. P. L. FARINAS, E. D. ORERO, R. PEREIRAS and F. S. PANISELLO, Arch. de med. inf. **7**:271 (April-June) 1938.

Two children with congenital cysts of the lung are presented. The first, a boy of 7 years, was discovered to have this condition during a roentgenographic study for osteomyelitis of the tibia. Two sacs were observed in the inferior lobe of the right lung. The boy died later of bronchopneumonia, and some interesting pathologic sections are shown. The second patient was a boy of 16 months. He had a suppurating cyst and was also suffering from pleurisy arising from acute pyodermitis. The regression of the pleural exudate revealed typical cysts.

SANFORD, Chicago.

TREATMENT OF PNEUMONIA WITH VITAMIN C. A. VOGL, München. med. Wchnschr. **84**:1569 (Oct. 1) 1937.

Vogl administered vitamin C to patients with pneumonia and patients recovering from operations which interfered with respiration (abdominal operations, rib resections, etc.) and were likely to be followed by pneumonia. He found the course of pneumonia shortened and less severe in comparison with pneumonia in similar cases in which vitamin C was not given. No specific serotherapy was used. Ascorbic acid was given in doses of from 200 to 500 mg. daily for a week. The 222 patients who had been operated on received from 100 to 300 mg. of ascorbic acid or the juice of two lemons daily as a prophylactic measure. There were no deaths due to pneumonia; 7 deaths were due to extrapulmonary factors and 6 patients experienced mild bronchopneumonia. Vogl urges the use of vitamin C in the treatment and prophylaxis of pneumonia.

BRAHDY, Mount Vernon, N. Y.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

THE ACUTE DIARRHEAL DISORDERS. A. V. HARDY and J. WATT, Am. J. Pub. Health **28**:730 (June) 1938.

On the basis of their observations in the Southwest, Hardy and Watt conclude that about 90 per cent of acute diarrheas are infectious and that a high percentage are due to infection with Shigella dysenteriae. A wider application of culture-taking demonstrates the fact that ideas of the clinical picture of dysentery arrived at by observation of hospitalized patients must be revised. In many cases the disease is mild. The authors present suggestions as to culture mediums.

LIMPER, Louisville, Ky.

CONGENITAL DIAPHRAGMATIC HERNIA. E. J. DONOVAN, Ann. Surg. **3**:374 (Sept.) 1938.

The symptoms of diaphragmatic hernia are the result of mechanical interference with the functions of the herniated viscera and with the functions of the respiratory and circulatory organs on which the disturbed viscera encroach; they are therefore respiratory or gastrointestinal or both. If the herniated viscera press on the heart or on the mediastinum, they may produce cyanosis, dyspnea and palpitation. If the large or the small intestine is involved, nausea, vomiting or an intestinal obstruction may result from crowding or kinking of the intestine. The symptoms vary to such a marked degree that the possibility of diaphragmatic hernia should always be kept in mind in the presence of respiratory difficulties pointing to involvement of the upper part of the abdomen or cardiac symptoms, the causes of which it is difficult to ascertain. Many of the patients are symptom free, and the hernia is discovered only by routine roentgenologic examination.

The diagnosis is most surely made by roentgenologic study.

Operative repair offers practically the only relief, and early operation is advised.

The author reports 10 cases. The report is illustrated with roentgenograms taken in each case.

BANTIN, Omaha.

PERSISTENT VOMITING IN EARLY LIFE (WITH SPECIAL REFERENCE TO OBSTRUCTIONS OF THE GASTROINTESTINAL TRACT). S. W. CLAUSEN, New York State J. Med. **38**:110 (Jan. 15) 1938.

Of 90 cases of severe vomiting in infancy which Clausen reports, 63.5 per cent were due to congenital obstructioin of the gastrointestinal tract. Six of the patients had obstruction of the esophagus, 29 pyloric stenosis and 14 an obstruction in the duodenum. Cardiospasm occurred in 10 and pylorospasm in 21. Duodenal obstruction occurred in 8 girls and 6 boys. Of these patients, 2 were mongolian idiots, 2 had hypospadias, 1 a cleft palate, 2 redundant sigmoid flexures, 7 cardiospasm and 1 mental retardation.

The symptoms, diagnosis and treatment of the various conditions are given. Surgical treatment was successful in 41 patients. Sixteen of the infants with organic obstruction died. A series of 21 older children with recurrent vomiting was also studied. Congenital partial obstruction was found in 4 and was probably present in 7. None had pyloric stenosis in infancy. The importance of close cooperation between the pediatrician and the surgeon is stressed.

AIKMAN, Rochester, N. Y.

COMMON PROCTOLOGIC DISORDERS IN CHILDREN. C. C. MECHLING, Pennsylvania M. J. **41**:886 (July) 1938.

Rectal examination is generally simpler and easier in a child than in an adult in spite of the lack of cooperation. After inspection of the external parts, digital examination is always indicated. A newborn child is not injured by the passage of an adult's little finger.

The anal canal is short, less than an inch long, and the rectum is straight, since the bend or curve of the adult sacrum has not yet been formed. Pain and bleeding are the common anorectal symptoms in children. The pain of ulcer causes the child to cry when he has a bowel movement, and blood may be seen in the feces. The ulcer is generally produced by the passage of hard feces which overstretch the anal wall. The ulcer is invariably located at the posterior position, since this is the weak arc in the anal circle. A perianal abscess is a common result of the presence of an ulcer. This abscess is to be noted on either side of the anus and is seen as a low rounded swelling, which is inflamed and tender. Bleeding is the other symptom which will defy treatment until the lesion provoking it has been detected. The most frequent cause of bleeding in children is a mucous polyp growing out of the mucous membrane. Blood is passed with the

feces and streaks them. Hemorrhages are uncommon. Malignant change in children is naturally rare. Rectal bleeding is an early sign in purpuric states. If the blood is fluid or bright red, its origin is in the rectum or in the part of the colon that is on the left side. If clotted blood is seen, its origin is in the part of the colon that is on the right side or the part that is in the middle of the abdomen. Hemorrhoids are not a common source of bleeding in infants.

Prolapse is a distressing phenomenon, usually seen in the marasmic child.

Constipation is a problem in pediatrics as it is in geriatrics. The desire or urge to defecate should be as natural as the urinary urge. When sufficient water is taken, the latter is easy, natural and frequent. The use of mineral oil, plain or in one of is many modified forms, is now the vogue in treating constipation. One is told that by its use feces are kept soft. When taken by mouth, it acts as a deterrant to absorption of water. It also interferes with ferment action and with absorption of the end products of digestion. Neither of these physiologic processes should be interfered with.

"Rectal feeding" is a misnomer, and the practice of rectal feeding has been practically discontinued. Only the end products of digestion, such as dextrose from the carbohydrates or amino acids from the proteins, are absorbed and made available for nutrition.

LOGUE, Williamsport, Pa.

MULTIPLE CONGENITAL ABNORMALITIES OF THE COLON. H. J. WARTHEN, South. M. J. **31**:528 (May) 1938.

Warthen reports a case of multiple congenital abnormality of the colon in a 7 year old boy. The anomalies included an imperforate anus, absence of the sphincter muscles, megacolon and arrested rotation of the colon.

The stricture was dilated, the incontinence was corrected by a Stone fascial transplant threaded through the adjacent gluteal muscles, and the megacolon was remedied by a bilateral lumbar ganglionectomy and ramisectomy.

SCHLUTZ, Chicago.

A CALCIFIED PRIMARY LIVER CELL CARCINOMA IN A FIVE YEAR OLD CHILD. H. J. HAMBURGER, Indian J. Pediat. **5**:98 (April) 1938.

Hamburger reports a case of circumscribed liver cell carcinoma (hepatoma) in a 5 year old child. There was associated cirrhosis. Scattered areas of calcification of the liver developed during the course of treatment with roentgen rays.

GONCE, Madison, Wis.

SUDDEN DEATH FROM VON GIERKE'S (GLYCOGEN) DISEASE. E. GARDNER and K. SIMPSON, Lancet **1**:659 (March 19) 1938.

Sudden death of a 3 month old breast-fed infant and of an 11 year old school boy from glycogenosis is reported. In each case death was unexpected, and at postmortem examination the heart muscle alone was seriously diseased. In each case the heart muscle fibers were of gargantuan dimensions, had imperfect transverse and longitudinal striations and showed foaminess of protoplasm. Glycogen was demonstrated in the boy's heart. It was not shown in the infant's heart, owing it was thought to the lapse of too much time, glycolysis having already taken place.

The medicolegal aspects of these occurrences are emphasized.

LANGMANN, New York.

A DIAGNOSTIC SIGN FOR RETROCECAL APPENDICITIS. E. ALTSCHULER, Lancet **1**:891 (April 16) 1938.

In all cases Altschuler has found one sign absolutely reliable, namely, decided tenderness and definite circumscribed muscle spasm localized over the right pelvic

margin. The sign is especially useful in diagnosing (1) acute retrocecal appendicitis before tenderness has appeared in the usual position, (2) a chronic, almost symptomless small abscess occurring after retrocecal appendicitis without operation and (3) long-standing chronic retrocecal appendicitis, which is generally diagnosed as colitis.

LANGMANN, New York.

HYPERTROPHIC PYLORIC STENOSIS IN ONE OF UNIOVULAR TWINS. W. SHELDON, Lancet **1**:1048 (May 7) 1938.

There are published records of hypertrophic pyloric stenosis in ten sets of twins. Unfortunately the type of twins was not always stated. With the exception of Lasch's case, the evidence indicates that when pyloric stenosis affects uniovular twins both infants show the condition.

In the case reported here a Rammstedt operation was performed. The healthy twin showed no symptoms or physical signs of pyloric stenosis.

LANGMANN, New York.

HEMORRHAGE AND INTESTINAL OBSTRUCTION DUE TO A MECKEL'S DIVERTICULUM. B. H. PAGE, Lancet **1**:1160 (May 21) 1938.

Meckel's diverticulum is found in about 2 per cent of people, most commonly in males.

There are four ways in which it commonly causes intestinal obstruction: 1. The diverticulum may become invaginated and thus cause an intussusception. 2. It may act as a band or noose over or through which a loop of intestine becomes strangulated. 3. Volvulus of a loop of intestine may be caused. 4. The bowel may be kinked or twisted at its point of attachment to the diverticulum.

A case is reported in a man aged 23. At operation the diverticulum was found attached by its blind end to the umbilicus and twisted several times in its long axis so that it was strangulated and almost gangrenous. It had caused a slight twist and kink of the ileum.

LANGMANN, New York.

CELIAC DISEASE. J. R. CAVALCANTI, Brasil-med. **52**:358 (April) 1938.

Cavalcanti reviews the history, causes, pathologic aspects and treatment of celiac disease and presents the case of a 5 year old girl. She presented classic symptoms and exhibited a glycemic curve that is pathognomonic, according to Haas. However, she was found to suffer from an infection with Ascaris lumbricoides. The author wonders if this might not account for her condition.

SANFORD, Chicago.

SEVERE VOMITING WITH ACETONURIA. LAEMMERHIRT, Deutsche med. Wchnschr. **64**:1218 (Aug. 19) 1938.

This dramatic vomiting occurs suddenly, mostly in children under 12 years of age. It may be a solitary attack, or in more severely neuropathic children it may become cyclic. The author thinks that this disease always starts with gastritis, leading to hypochlorhydremia, which is associated with interruption of the utilization of glycogen from the liver. This abnormal condition of chloride loss and glycogen starvation manifests itself on the nervous system and can be recognized by the irresistible vomiting, the thirst and the excessive amount of acetone in the urine.

The purpose of therapy is to stop the vomiting, to allay the thirst, to stop the carbohydrate starvation and to calm the nervous system.

The author suggests that 330 cc. of a 5 per cent dextrose solution mixed with from 3 to 5 drops of tincture of opium be administered hourly by rectum. An injection of phenobarbital is also advisable. The author chose dextrose because of its easy assimilability and opium for the purpose of obtaining better retention of fluids by rectum and for its calming effect on the vegetative nervous system.

The phenobarbital has a sedative effect on the central nervous system and also on the endocrine glands. With this method of treatment he succeeded in all cases of true cyclic vomiting in controlling the thirst and vomiting in twelve hours and in stopping the disease completely in twenty-four hours. He does not think that psychotherapy is important in the management of patients with this disease.

KERESZTURI, New York.

CELIAC DISEASE. F. KUHLMANN, Monatschr. f. Kinderh. **73**:367 (June) 1938.

This verbose article describes a case of celiac disease. Photographs and a roentgenogram of the involved part of the intestine are reproduced. There was no osteoporosis.

GERSTLEY, Chicago.

ROENTGENOLOGIC ASPECTS OF INTESTINAL MOTILITY IN CASES OF DYSENTERY AND ENTEROCOLITIS. S. PINELES, Bull. Soc. de pédiat. de Iasi **8**:25 (Jan.-June) 1937.

Fourteen cases were studied by means of roentgen rays and a barium sulfate meal. It was found that in many cases the interference with normal peristalsis was due to localized spasm of the intestinal musculature. Three illustrations show numerous localized masses of barium sulfate proximal to the area of spasm.

LESLIE, Evanston, Ill.

GASTRIC RUPTURE IN CHILDREN. J. VAVRDA, Bratisl. lekár. listy **16**:217 (May) 1936.

A discussion of traumatic and of spontaneous rupture of the stomach is followed by a review of the literature, which reveals that 2 cases of traumatic rupture in children have been recorded, and no case of spontaneous rupture. The author reports the case of a boy of 9 years who suffered a traumatic rupture of a full stomach on falling down stairs. Operation was performed within four hours, and a transfusion was given, but the boy died within an hour after operation. This patient had a complete rupture through the anterior portion and an incomplete tear through the serosa posteriorly.

STULIK, Chicago.

ATRESIA OF THE COMMON BILE DUCT IN INFANCY. H. HUMBURSKY, Bratisl. lekár. listy **16**:340 (July-Aug.) 1936.

Humbursky gives a résumé of the etiology, embryology, mechanics, anatomy and symptoms. The case reported was that of a boy 3 months of age with a classic icterus complex. At autopsy the following conditions were noted: atresia ductus choledochi, biliary cirrhosis of the liver, stenosis of the cystic duct, hypoplasia vesicae fellae, icterus gravis, tumor lienis chronicus, enterorrhagia diffusa, punctiform hemorrhages of the pleura and pericardium, pulmonary edema and anemia gravis. This seems to belong to the group of Rolleston-Hayne, in which the icterus develops secondarily and not congenitally, i. e., primary cirrhosis and secondary atresia.

STULIK, Chicago.

TREATMENT OF INFANTILE DIARRHEAS IN GENERAL PRACTICE. J. SVEJCAR, Časop. lék. česk. **75**:914 (July 17) 1936.

Svejcar discusses the dietary disturbances of infancy from the standpoint of diet, infection, supply of vitamins and allergy. The outlined treatment includes preliminary starvation, followed by a feeding of rice water and then toast, breast milk, high calcium milk, buttermilk and albumin milk. The important point to keep in view is the reestablishment of tolerance for the various types of food. The feeding schemes employed in several cases are given in detail.

STULIK, Chicago.

A Peculiar Case of Glycogenic Enlargement of the Liver. J. J. Neuteboom, Maandschr. v. kindergeneesk. **7**:233 (March) 1938.

Neuteboom gives the history and describes the clinical course of an illness in a boy of 13 years. The diagnosis, hepatomegalia glycogenica, was based on the results of a biopsy. Changes in the metabolism such as those which the abstracter described many years ago in his 2 patients with glycogenic enlargement of the liver were absent in Neuteboom's patient. This may have been due partly to the fact that the latter's patient was not examined before the age of 13 years. Another possibility is that he dealt with a condition totally different from glycogen disease. His patient reacted favorably to a diet poor in carbohydrates and rich in fat. As regards the etiology of glycogenic enlargement of the liver Neuteboom is inclined to accept prenatal or natal injuries at definite places of the spinal marrow. Some experiments in rabbits are presented in favor of this conception.

van Creveld, Amsterdam, Netherlands.

Cascade Stomach in an Infant. M. C. M. Oltmans-Smid, Maandschr. v. kindergeneesk. **7**:292 (April) 1938.

A boy 3 months old vomited when larger quantities of food were given. The vomitus, however, did not consist of food but of a slimy colorless fluid which practically did not contain free hydrochloric acid. Roentgen examination of the boy in different positions showed that he had a cascade stomach.

van Creveld, Amsterdam, Netherlands.

Acute Intoxication in Babies. J. Munk, Nederl. tijdschr. v. geneesk. **82**:611 (Feb. 5) 1938.

This is a clinical lecture in which the present treatment of acute intoxication and the experiences with this treatment in the pediatric clinic of Leyden, Netherlands, are given.

van Creveld, Amsterdam, Netherlands.

Nervous Diseases

Operative Treatment of Communicating Hydrocephalus. W. E. Dandy, Ann. Surg. **108**:194 (Aug.) 1938.

The purpose of this paper is to show the effect of further operative removal of the choroid plexus from the brain when removal of the glomus from each side has been found to be inadequate. Dandy gives his operative technic and reports 2 cases.

Unless hydrocephalic children are brought for treatment very early, attempts at cure are not worth while. For the rapidly growing hydrocephalic child, 3 months of age is the outside limit for surgical intervention; for the patient who is growing less rapidly, the limit may vary from 6 months to 1 year. The earlier the treatment the better are the results in terms of life and of subsequent mentality. Since the brain is so rapidly destroyed by advancing hydrocephalus, it is important that delay be avoided when further surgical efforts are to be instituted.

Bantin, Omaha.

Experimental Investigations in Hemorrhagic Encephalitis. A. B. Baker and C. W. Buggs, J. Infect. Dis. **62**:293 (May-June) 1938.

Fresh brain tissue from a patient who died of hemorrhagic encephalitis proved very infectious for rabbits on intracerebral inoculation. Guinea pigs and white mice did not react to the infectious agent.

The active agent was passed serially through 16 sets of animals before it was lost. All animals presented a characteristic picture of involvement of the central nervous system, consisting of hyperirritability, muscular twitchings, motor weakness, convulsions and moderate salivation.

The active agent lost its potency when stored in 50 per cent glycerol at 0 C. for one month. One instance is noted in which the active agent proved infectious on subcutaneous inoculation. Attempts to filter the infectious agent proved unsuccessful.

The brains of rabbits inoculated with the infectious agent revealed changes quite similar to those found in the brains of persons who died of hemorrhagic encephalitis.

TOOMEY, Cleveland.

MIGRAINE AND EPILEPSY: NEWER CONCEPTS AND TREATMENT. W. G. LENNOX, J. Med. **19**:284 (Aug.) 1938.

The electroencephalogram has been useful in the study of epilepsy. The article on this subject by Lennox may be summarized as follows:

A seizure is accompanied by a disturbance of the normal electrical activity of the brain. The three types of seizures have distinct cerebral rhythms.

Seizures which are subclinical are often registered in the electrocephalogram. An approaching grand mal seizure probably can be predicted many hours before its arrival. The point of origin of the abnormal rhythm can be determined if it is situated in the cortex. On the basis of such electroencephalographic evidence, frontal lobectomy was performed in 3 patients, with excellent results in 2 of them.

The effect of treatment can be promptly visualized.

NELSON, Cincinnati.

ETIOLOGY OF CHOREA. C. H. SCHRODER, Minnesota Med. **21**:322 (May) 1938.

Schroder presents the observations of more than 30 authors on the subject of chorea. His conclusion is that "it does not seem possible in the present state of knowledge to make the dogmatic statement that chorea is dependent on an infectious process, or, on the other hand, that it is not related to infection." He does not defend either view but simply presents the evidence.

ANDERSON, Minneapolis.

THE BRAGG-PAUL PULSATOR IN THE TREATMENT OF RESPIRATORY PARALYSIS. C. J. MCSWEENEY, Brit. M. J. **1**:1206 (June 4) 1938.

McSweeney describes an apparatus to be used in the treatment of patients with various forms of respiratory paralysis. It consists of a distensible rubber bag, which is applied around the patient's chest in the form of a belt and which is rhythmically filled with and emptied of air by means of a bellows. Electric power is used.

It is of special benefit when used on patients with postdiphtheritic respiratory paralysis and anterior poliomyelitis. The author reports unusual success in its use.

ROYSTER, University, Va.

PURULENT MENINGITIS: NINE CONSECUTIVE CASES WITH SEVEN RECOVERIES. J. ADAM and E. A. M. CONNAL, J. Laryng. & Otol. **52**:87 (Feb.) 1937.

This series of 9 consecutive cases of purulent meningitis complicating suppuration of the middle ear, with 7 recoveries, interested Adam and Connal because their previous experience had been one of uniform failure. An analysis of 623 cases of meningitis (other than meningococcic or tuberculous), mainly following otitis or sinusitis, by Neal, Jackson and Appelbaum showed only 16 recoveries (about 2.5 per cent), and Neumann during six years had 22 recoveries (37 per

cent) in 59 cases. Only a single successfully treated patient was over 15 years of age. In the present series of 9 patients, 6 were over 15, of whom 5 recovered. The total recovery rate was 77 per cent, but of course 9 is far too small a number to serve as a basis for ratios. Of the patients who died, one was in a hopeless condition on admission, and the other would probably have been saved by better technic. Further, whereas Neumann did not open the dura, the authors have done so without exception. The experience of one of them in 2 previous cases suggested dural incision. This was done, together with regular lumbar puncture and in 5 cases with the injection of air, from 10 to 30 cc., through the lumbar needle, in accordance with Mayer's suggestion. Incision seems to have been helpful; certainly it has done no harm. Less cerebrospinal fluid exudes on the whole, than was anticipated, because the intracranial pressure thrusts the brain against the incision. The authors give brief histories of the 9 cases.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

INFANTILE CONVULSIONS. R. W. B. ELLIS, Practitioner **140**:407 (April) 1938.

In an infant or a young child a convulsion may be of minimal importance or may be the prelude to a severe and fatal illness. The attack may vary from momentary deflection of the eyes upward, with rigidity or twitching of a limb, to prolonged violent clonic movements, passing on to status epilepticus, coma and death. Convulsions should be regarded as essentially symptomatic—the reaction of a relatively immature and unstable central nervous system to a large number of stimuli—and though certain general principles of therapy will apply to the immediate attack, treatment must ultimately be based on an understanding of the cause.

Both general and specific treatments are discussed with regard to the neonatal period and later infancy. Asphyxia of the newborn, maternal eclampsia, allergy to milk, tetany of the newborn and tetanus are included as etiologic factors in the neonatal group. Infections, disturbances of metabolism, metallic and other poisons, congenital cerebral defect, peripheral irritation and idiopathic epilepsies appear among the factors in later infancy. C. F. GELSTON, San Francisco.

A FURTHER CASE OF THE AMSTERDAM TYPE OF DEGENERATION. C. DE LANGE, Arch. de méd. d. enf. **41**:193 (April) 1938.

Under the designation "typus Amsteodamensis" de Lange reported, in 1933, 2 cases of a new form of degeneration found in Holland. Since that time there have been 2 further observations published, and in the current contribution another instance of the unusual syndrome is described, with a complete report of the observations at autopsy.

Characteristic features of the disorder appear to be: a short incurved little finger such as one finds in mongolism; syndactylism; saddle nose, and micromelia. The pattern of the palmar creases resembles that found in the monkey; there is contracture of the elbow, and the diaphyses of the radius and the ulna are abnormally large and heavy.

AMESSE, Denver.

A CASE OF ASTASIA-ABASIA IN CHILDHOOD. C. T. SIMON, Méd. inf. **9**:134 (May) 1938.

Astasia-abasia is characterized by a sudden incapacity of the subject to stand or walk with complete lack of organic lesions to justify the motor symptoms. The case of an 11 year old boy in whom this hysterical neurosis developed is reported. When he was standing, his knees would give way and he would slowly fall to the floor; however, in the supine position, his muscle action was normal. Neurologic and physical examination demonstrated no abnormalities except pain on pressure in the popliteal space. The boy showed normal intelligence according

to the Binet-Simon tests. After eleven days in the hospital he was well. In the endeavor to find a cause nothing pertinent was brought to light except some dissatisfaction with the amount of work required of him at school.

HIGGINS, Boston.

PRECOCITY, HALLUCINATIONS AND NARCOLEPSY FOLLOWING ENCEPHALITIS. J. LHERMITTE, Rev. neurol. **69**:65 (Jan.) 1938.

A boy of 14 years began to show somnolence six months after otitis media and facial paralysis. His weight increased rapidly, and his genital organs matured. He had nightmares. He found it difficult to execute voluntary movements rapidly. There were two attacks of narcolepsy. His mentality seemed intact, but he was socially maladjusted.

Lhermitte believes this case proves that the hypophysis can be directly involved in an encephalitic process.

DAFFINEE, Boston.

INFANTILE ENCEPHALOPATHY (FORSTER TYPE). M. E. MANTERO and M. ARIAS, Arch. de pediat. d. Uruguay **9**:20 (Jan.) 1938.

The case of a boy 5 years old is reported. He showed muscular hypotonia when recumbent and choreoathetosis, hypertonicity and absence of reflexes when in the vertical position. Idiocy was also present. The general manifestations resembled the syndrome of Forster.

SCHLUTZ, Chicago.

SYDENHAM'S CHOREA IN VARIOUS MEMBERS OF A FAMILY. D. CORREA and A. P. VARELA, Arch. de pediat. d. Uruguay **9**:51 (Jan.) 1938.

The authors report a family of 9 members, among whom the mother and 7 children presented traumatic fever. Of the 7 children, 4 acquired chorea.

SCHLUTZ, Chicago.

A TYPICAL CASE OF LYMPHOCYTIC MENINGITIS. R. TOLEDO and C. MARQUES DIAS, Arch. de pediat., Rio de Janeiro **10**:455 (June) 1938.

The child was 11 years old and irrational. Kernig's sign was present. The spinal fluid showed 60 cells, 95 per cent of which were lymphocytes. The child's recovery was uneventful.

SANFORD, Chicago.

WILSON'S DISEASE IN TWO SIBLINGS. HEINRICH SCHWYN, Schweiz. Arch. f. Neurol. u. Psychiat. **40**:221, 1937.

Schwyn states that Wilson's disease occurs most frequently in large families and that a single case in one family is rarely encountered. Although the age at onset usually falls between the seventh and the fifteenth year, the malady has been known to appear as late as the fourth decade. The course is generally more rapid in younger patients. The 2 patients whose histories are reported had 14 brothers and sisters, 3 of whom died in infancy. The oldest sister and a maternal aunt were patients in hospitals for mental disease; a maternal uncle had epilepsy. The father, though a good worker, was quiet and peculiar. Both patients made good progress in school and subsequently were industrious. The first, a woman aged 22, presented as initial symptoms marked fatigability, stubborn insomnia, inappetence and unsteadiness of gait. After about three weeks, loss of facial expression and stooped posture were noted. The prevailing mood from the beginning was one of depression; the patient became apathetic, expressed ideas of poverty and made two attempts at suicide. On examination, ten months after the onset, seborrhea of the face, stiffness in mimetic movements, with the features set in a fixed smile, and psychomotor retardation were observed. Speech was slow and

monotonous; chewing and swallowing were difficult; movements of the extremities were slow and awkward, and there was a fine tremor of the hands. The patient was unable to care for herself and had incontinence of urine. About fourteen months after the onset, she became acutely ill with fever and abdominal pain and died in a few days. Autopsy revealed, in addition to serofibrinous peritonitis, a grossly nodular liver, chronic swelling of the spleen and punctate hemorrhages in the region of the basal nuclei. The hemorrhages were most numerous in the corpus striatum, which presented other grossly visible changes. Microscopic examination of the tissues is not reported.

The second patient, a younger brother of the first, on entering military service in his nineteenth year seemed tired and lacking in energy. He had a seizure, which was thought to be hysterical, and it was subsequently learned that he had become depressed and apathetic several months before this attack. On return from service two months later, changes in character were evident; he was restless, excitable, given to silly jokes, sexually aggressive and alternately depressed and elated. Several months later, during a period of vagrancy, he fell frequently, finally injuring himself; on his return home his face was masklike, and he showed little interest in his surroundings. In spite of the increasing physical and mental disability, however, he found employment and later served the required two weeks with the militia. When he was examined nearly two years after the onset, his face was greasy and expressionless, his speech slow and monotonous and his posture stooped. The muscles of the extremities were rigid, and there was a fine tremor of the hands. Examination of the corneas with a slit lamp disclosed a pigmented ring in Descemet's membrane. Formal tests revealed no defect of intelligence, but the patient was depressed and tearful; there was general slowing of the mental processes, and the behavior was characterized by childish indifference. A mixture of scopolamine and atropine afforded no symptomatic relief. The patient died, apparently of septicemia complicating cellulitis of the forearm, two and one-half years after the onset. A firm, finely nodular liver and chronic swelling of the spleen were observed at autopsy. There was slight atrophy of the frontal lobes with more marked atrophy of the putamen of both sides. Microscopically, there was extensive destruction of both small and large ganglion cells in the putamen, with glial proliferation, deposits of fat in gitter cells and lying free in the tissues and marked increase in iron content. The numerous blood vessels, mainly precapillaries, in the caudal portion of this structure were surrounded by scavenger cells and in places by lymphocytes and polymorphonuclear leukocytes. Large glia cells of Alzheimer type I and clumps of somewhat smaller cells, corresponding to Alzheimer type II, were seen in the putamen. Similar, but less pronounced, glial changes, with occasional perivascular infiltrations, were seen in the caudate nucleus, corpus Luysi and substantia nigra. The cerebral cortex, particularly the third and fifth layers, showed glial alteration and a few cells of Alzheimer type II. Changes in ganglion cells with moderate proliferation of glia were noted in the dentate nucleus and in Bergmann's layer of the cerebellar cortex.

Schwyn expresses the view that in the cases reported here it is possible that a tendency to mental disturbance was inherited with the recessive anlage for Wilson's disease and that the latter condition merely served to precipitate the psychosis.

DANIELS, Denver. [ARCH. NEUROL. & PSYCHIAT.]

A NEW ASPECT OF EPILEPSY. D. M. VAN LONDEN, Nederl. tijdschr. v. geneesk. **82**:846 (Feb. 19) 1938.

After a thorough study of 1,600 epileptic patients, van Londen concludes that the stimuli giving rise to epilepsy and related conditions must have an exogenic origin. These stimuli, which have a special character and do not act on the normally functioning cerebral system, penetrate into this system in the epileptic patient because in this patient the protective apparatus of the system is impaired.

The onset of the epileptic attack depends on the localization of the defect in the protective apparatus. So, according to the author, epilepsy and related conditions are not manifestations of a disease of the central nervous system but are warning signals which announce the presence of dangers to this system.

VAN CREVELD, Amsterdam, Netherlands.

CEREBRAL COMPLICATIONS. C. DE LANGE, Nederl. tijdschr. v. geneesk. **82**:3540 (July 16) 1938.

In this clinical lecture de Lange gives the history of three patients. The first patient was a boy of 10 years, suffering from typhoid fever. He presented choreic movements—a very rare complication. The second patient suffered from encephalitis and pneumonia, followed by empyema, developing after measles. The third patient had acute hemorrhagic nephritis, followed by temporary paralysis of the right facial and hypoglossal nerves and by motor aphasia, without change in the spinal fluid. Probably these complications were caused by local cerebral edema.

VAN CREVELD, Amsterdam, Netherlands.

Psychology and Psychiatry

AN ABNORMAL CHILD. E. STERBA, Psychoanalyt. Quart. **5**:375 and 560, 1936.

Sterba reports fully the symptoms, analysis and psychic mechanisms of an abnormal boy aged 5. His illness showed an essential difference from a childhood neurosis. Despite his unusual intellectual maturity, the abnormality consisted in his adhering to an early stage of ego development in relation to reality. Although a minor number of constituents of his ego had developed a relation to reality, the chief components remained retarded because of severe traumas which he had suffered in his second and third years and because of his pathologic self love and strong oral fixation. He was defective in reality tests and was convinced that reality consisted in what he asserted or imagined. Because of his frustrations and injuries, his picture of reality had undergone alteration in such a way as to protect him against all dangers. Certain of his symptoms resembled those of a compulsive neurosis, but whereas in the latter the symptoms are formed unconsciously, in this case all the ritualistic behavior was devised consciously and against dangers which the boy knew exactly. His psychosis differed from an adult psychosis, since the essential character of the latter is loss of contact with reality. This child had failed to acquire any such relationship at all; i. e., there was no regression because there was nothing to which to regress.

The aim of treatment differed from that for a childhood neurosis. It was a question not of discovering and making intelligible the unconscious but of permitting the boy to make up for his deficient contact with reality—to educate him to a normal sense of reality. Through this, he began to develop object relationships, which became gradually stronger, and his libidinal orientation underwent alteration, for he became freed in part from his oral fixation.

PEARSON, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

STORY COMPLETION AS A METHOD FOR DETECTION OF AFFECTIVE COMPLEXES AND CONFLICTS IN CHILDREN. M. THOMAS, Arch. de psychol. **26**:209 (Dec.) 1937.

Thomas critizes the two methods now used by a majority of medicopedagogic counselors, namely, the direct interview and psychoanalysis. In her opinion the former arouses considerable resistance in the child, while the latter takes too much time. She suggests that use be made of a battery of short stories to be completed by the child. The underlying assumption is that each child is likely to consider a story of the type selected in the light of his or her own emotional conflicts and complexes, thus enabling the examiners to detect both the source

and the causes of the trouble. The application of the method to two groups of children showed that (*a*) in 90 per cent of the cases the results were in complete agreement with the actual situations of the subjects involved, (*b*) in 3.6 per cent the results did not seem to be substantiated by the facts, and (*c*) in 6.4 per cent it was impossible to secure definite pictures for the children studied.

GOBEY, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

DIAGNOSTIC VALUE OF DRAWINGS BY PROBLEM CHILDREN. T. TRAUBE, Arch. de psychol. **26**:285 (Dec.) 1937.

This study is based on the assumption that a child in drawing gives unconsciously a synthesis of his or her inner self. Traube studied a large number of drawings made by two groups of problem children. He interpreted the drawings made by the children in the first group after personal interviews with the children. The drawings made by the subjects in the second group he interpreted independently and later verified the interpretations in personal interviews. The results thus obtained he compared with those for a group of normal children of the same ages and found them to be significant for the purposes of diagnosis.

GOBEY, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

PSYCHOMOTOR CORRELATIONS IN NORMAL SCHOOL CHILDREN. J. ABRAMSON and S. LE GARREC, Hyg. ment. **32**:1 (Jan.) 1937.

Abramson and Le Garrec attempted to correlate motor skills with the standard intelligence ratings of a number of normal school children. They found insufficient motor activity in the following groups of pupils: intellectually normal, intellectually superior and intellectually subnormal. They found also that pupils of superior intelligence often have inadequate motor skills.

ANDERSON, Los Angeles. [ARCH. NEUROL. & PSYCHIAT.]

PSYCHOLOGY OF CHILDREN'S MINOR AILMENTS. A. BUTAVAND, Rev. méd.-sociale de l'enf. **5**:350 (Sept.-Oct.) 1937.

The minor psychologic disturbances of children, particularly when they are subjected to trivial illnesses while in strange surroundings, have interested the author. The case histories of 3 infants so afflicted are presented.

DIETRICH, Beverly Hills, Ill.

THE RELATION BETWEEN MENTAL DISTURBANCES AND DISORDERS OF SPEECH: I. DISTURBANCES IN NAMING AND PARAPHASIA. E. STENGEL, Monatschr. f. Psychiat. u. Neurol. **95**:129 (April) 1937.

Stengel studied the effects of certain general mental alterations on the function of speech in a group of 6 patients suffering from cerebral vascular disease and post-traumatic and postepileptic mental disorders. All the patients showed disturbances of consciousness and an amnesic syndrome of the Korsakoff type, though confabulations were not as a rule prominent. All had difficulty in naming objects, perseveration and paraphasic symptoms. They found abstract problems more difficult to solve than concrete ones. There was little spontaneous speech, but understanding of speech was not impaired. The difficulty in naming objects differed from that associated with amnesic aphasia, as the patients freely substituted incorrect names and seemed unaware of their errors. They often used names which had just been heard but which bore no relation to the object. Some mistakes owed their origin to perseveration; other faulty responses were characterized by the use of neologisms. The following types of paraphasic disturbances were distinguished: one, in which perseveration played a role; another, in which a tendency to flight of ideas was observed, and yet another, in which confabulatory

tendencies were noted. Mixtures of these three types were encountered in some cases.

From a descriptive point of view, the disorder of speech was regarded as an atypical aphasic disturbance, with the paraphasia placing it in the group of sensory aphasias. It was thought that the altered state of consciousness and the associated impairment of thought were largely responsible for the aphasic symptoms. A disorder of attention was probably the most important factor in producing the disturbance of thought. This explains the resemblance between the mistakes made by these patients and those observed in normal persons who are fatigued and inattentive. The general attitude of the patients toward speech also played a role in the aphasic symptoms. They were disinclined to talk or to use speech for the purpose of designating objects to which their attention was called. They showed a tendency to finish the task in the easiest and quickest manner possible, wishing to avoid the effort necessary to overcome their slowness of thought and impaired comprehension. The disorder of speech showed certain features which were reminiscent of the flight of ideas in manic states and of the neologisms observed in schizophrenia. From the attitude of the patients it was evident that their contact with the ouside world was faulty. In this respect they resembled patients with schizophrenia. They tended to ignore the acquired knowledge of the relation between word and concept; as a result, their speech resembled that of children learning to talk. Further similarities to the speech of children were noted in the stubborn manner in which the patients defended their incorrect responses and in the frequency with which they echoed the words addressed to them. Stengel discusses the much disputed question whether aphasic conditions should be attributed to general psychic alterations or to disturbances of functions primarily concerned with speech. He believes that both these mechanisms are frequently operative, though there are extremes in which one or the other may be completely in the foreground.

ROTHSCHILD, Foxborough, Mass. [ARCH. NEUROL. & PSYCHIAT.]

Diseases of the Genitourinary Tract

SULFANILAMIDE IN THE TREATMENT OF GONORRHEAL VULVOVAGINITIS. S. J. HOFFMAN, M. SCHNEIDER, M. L. BLATT and R. D. HERROLD, J. A. M. A. **110**:1541 (May 7) 1938.

Twenty-five children afflicted with gonorrheal vulvovaginitis were given courses of sulfanilamide therapy. The authors review the results which they obtained with methods previously in vogue and the results of others for comparison. Two courses cured 16 of the 25 children, as indicated by two negative smears a week apart and the results of later follow-up examinations.

HEERSMA, Kalamazoo, Mich.

TREATMENT OF GONOCOCCIC VAGINITIS WITH THE ESTROGENIC HORMONE. R. W. TELINDE, J. A. M. A. **110**:1633 (May 14) 1938.

TeLinde reports that 335 children were cured of gonococcic vaginitis by treatment with an estrogenic substance extracted from amniotic liquid (amniotin). This estrogenic substance was either injected in oil or inserted into the vagina in the form of a suppository. Of the 175 children treated by injection, 75 per cent were cured; of the 160 children treated by insertion of the suppository, all were cured. On the average, the response of vaginal hyperplasia, desquamation and acidification occurred within two weeks after beginning the daily instillation of from 400 to 800 units vaginally. This treatment was continued two weeks beyond the date of the first negative smears. No ill effects seem likely to occur. Examinations after from three months to two and one-half years showed 98 per cent of the children well. TeLinde thinks that vaginitis was probably the only lesion present in these patients.

HEERSMA, Kalamazoo, Mich.

INTRA-ABDOMINAL CRYPTORCHIDISM TREATED WITH GONADOTROPIC SUBSTANCE. G. B. DORFF, J. A. M. A. **110**:1799 (May 28) 1938.

Eleven boys with one testis retained within the abdomen and a twelfth boy with both testes retained were treated with large doses of gonadotropic substance over varying periods. Descent occurred in 9—descent to the scrotum in 1 and descent to the canal in 8. The accompanying genital hypoplasia was relieved, but anomalies were not affected. Suprapubic hair developed, but later fell out except in older boys. Treatment should be begun early, and Dorff feels that further descent will be obtained by the same therapy. Subsequent examination revealed no case in which there had been recession of improvement.

HEERSMA, Kalamazoo, Mich.

PRECOCIOUS SEXUAL DEVELOPMENT FROM AN ANTERIOR PITUITARY-LIKE PRINCIPLE. W. O. THOMPSON and N. J. HECKEL, J. A. M. A. **110**:1813 (May 28) 1938.

Of 33 patients treated for undescended testes with the gonadotropic substance obtained from the urine of pregnant women, 18 showed genital growth. The characteristic changes were hypertrophy of the genitalia, excepting the testes, growth of hair, change in voice and frequent erections. Basal metabolism was affected little. Four cases are presented, with measurements and photographs. Usually testicular descent occurred along with genital hypertrophy but not always. Thompson and Heckel feel that the gonadotropic substance used is indicated for cryptorchidism, but that treatment should be stopped before genital hypertrophy becomes marked.

HEERSMA, Kalamazoo, Mich.

SYMPTOMS, DIAGNOSIS AND TREATMENT OF RENAL CYSTS. R. M. LECOMTE, South. M. J. **31**:632 (June) 1938.

Patients with renal cysts who exhibit only medical symptoms, e. g., signs of nephritis or of hypertension, require symptomatic treatment of a strictly medical nature. They have been submitted to surgical procedures, such as puncture of the cysts, decapsulation and so on, but apparently without any arrest of the progressive formation of cysts or the squeezing out of the functioning urinary tubules. Puncture of the cysts may, however, have a beneficial effect on the symptoms, both general and local, and the tendency now is to operate on patients with regard to whom a conservative attitude has for a long time been observed.

If nephrectomy is contemplated, and the need for it may arise unexpectedly in almost any renal operation, the patient should be assured of a sufficient functional reserve in the kidney that may have to be left behind.

SCHLUTZ, Chicago.

ALKAPTONURIA IN A NURSLING. U. S. RUZICIC, Monatschr. f. Kinderh. **73**:195 (May) 1938.

This makes the forty-sixth case of this condition to be reported since 1920. In 33 of the reported cases, the condition was congenital. In the majority of reported cases the patients were males and often siblings. In this instance the condition was observed in a girl. As in many of the cases reported, the child's parents were related.

GERSTLEY, Chicago.

INVESTIGATIONS OF METABOLISM IN CHILDREN WITH ALKAPTONURIA. E. SCHMIEDING, Monatschr. f. Kinderh. **73**:216 (May) 1938.

In 2 children with alkaptonuria, Schmieding made experimental studies of metabolism as well as of oxidation of blood serum in the test tube. He concludes that the origin of the alkaptonuria is in the liver. His procedure was to deter-

mine the effect of large doses of thyroid extract on the excretion of nitrogen, comparing this with the excretion of the alkaptone derivatives. He suggests that preparations of liver should be of value but has been unable to demonstrate any favorable effect.

GERSTLEY, Chicago.

PYELOCYSTITIS IN INFANTS. M. HANZL, Časop. lék. česk. **75**:726 (June 5) 1936.

In addition to intramuscular injections of eucystin (hexamethylentetraminum camphoricum) Hanzl advises a diet little productive of putrefaction. For infants she advocates farinaceous feedings with no or little milk and for older children farinaceous puddings with addition of milk, butter and eggs. In the presence of an alkaline urine, she uses phosphoric acid. A short résumé of the history, etiology, symptomatology and diagnosis of the condition is given.

STULIK, Chicago.

Diseases of the Ductless Glands; Endocrinology

CLINICAL INDICATIONS FOR ANTERIOR PITUITARY-LIKE SEX HORMONE. R. L. SCHAEFER, E. A. SHARP and J. V. LAMMY, Endocrinology **22**:643 (June) 1938.

In 16 cases of genital hypoplasia and cryptorchidism, 15 cases of amenorrhea and 13 cases of menometrorrhagia the gonadotropic substance from the urine of pregnant women gave almost uniformly good results. The authors look on the gonadotropic hormone found in the urine as the maturing factor of the gonads.

JACOBSEN, Buffalo.

ANTIHORMONE STUDIES IN BOYS TREATED WITH ANTERIOR PITUITARY-LIKE HORMONE FOR GENITAL UNDERDEVELOPMENT. G. B. DORFF, Endocrinology **22**:669 (June) 1938.

From a group of 19 boys who had received a potent gonadotropic substance derived from the urine of pregnant women for varying degrees of genital underdevelopment, 20 specimens of serum were taken and studied for the presence of a factor antagonistic to the gonadotropic substance, i. e., an antihormone, which might have resulted from chronic treatment. These tests showed that in all cases the serum was free from antihormone.

The author considered that a lag in response to treatment was due to need for increased doses or to the possible development of tolerance to one particular brand of the gonadotropic product. He believes that failure to secure descent of testes when a proper dosage is used is always an indication of mechanical obstruction.

JACOBSEN, Buffalo.

PITUITARY DWARFISM: TREATMENT WITH GROWTH HORMONE. N. M. TAYLOR, Endocrinology **22**:707 (June) 1938.

Eight patients with deficiency of the endocrine growth factor (pituitary dwarfism) were treated with an extract of the anterior lobe of the pituiatry containing the growth factor. The resulting growth was from double to five times that expected. Behavior problems became adjusted satisfactorily during the period of treatment in 5 of 7 patients. (The concomitant administration of thyroid to all the patients makes it difficult to estimate the role played by the growth factor.) No phenomena were noted by which one could postulate the occurrence of a period during which a patient was refractory to treatment or the occurrence of an antihormone.

JACOBSEN, Buffalo.

RECOGNITION AND TREATMENT OF ADOLESCENT ENDOCRINE DISTURBANCES. F. B TALBOT, M. Clin. North America **22**:805 (May) 1938.

Certain conditions such as cretinism, myxedema, goiter, diabetes and parathyroid tetany are fairly well understood and admit of rational treatment. The nature of many other syndromes can as yet only be conjectured and must await, for their interpretation, such time as the circulating hormones of glands may be measured and their actions and interactions determined. The problems of endocrinology are complicated by the fact that hardly any physiologic reaction is known to belong specifically to an individual gland. The diagnostic approach to these conditions must be made along two lines: clinical observation and laboratory study.

On the clinical side, the observation of disturbances of growth is of great importance. However, before drawing any conclusions, a careful study of the normal physiology and variations of growth is necessary if errors are to be avoided. For instance, early superior growth may only anticipate the normal growth which will come later. Hereditary peculiarities and tendencies must also be given consideration. Therefore only by prolonged study and observation should definite conclusions be drawn. As a basis for study it may be assumed that gigantism in the child and acromegaly in the adult are due to oversecretion of the pituitary gland. Conversely, deficient growth, or dwarfing, results from deficient pituitary functioning and hypothyroidism. In the latter group a consideration of nutritional factors must not be neglected. Abnormal growth of separate parts should be considered, such as shortening of the arms and legs in cretinism. Hypothyroidism is characterized by delayed ossification, while the centers appear at the normal time in pituitary dwarfism.

In the realm of sex development, much has been written and little is proved. The gonadotropic hormone of the anterior lobe of the pituitary is held to be the most important element in sex development, although the pineal gland, adrenal renal cortex and gonads must be considered in differential diagnosis. That cryptorchidism in a certain proportion of cases is due to a disorder of the pituitary gland is attested by clinical and therapeutic experience.

Probably most children showing so-called obesity are either normal or not actually obese. Clinical findings should be compared with the urinary creatinine for an accurate picture of the relative body makeup of fat and muscle. The influence of the pituitary on the metabolism of carbohydrate and fat may have some bearing on obesity, especially when combined with deficiency of the gonads. Disturbances of the thyroid gland do not cause true obesity, in which the relative amount of fat in the body is increased, but myxedema.

In the study of basal metabolism in children, the values obtained for those with normal physical development can be compared with almost any standard, but the obese or underweight child should be investigated by special methods. Any standard which includes weight in its formula, as do both the body surface and the multiple prediction formulas, will give seemingly low figures in cases of obesity and high figures in cases of malnutrition. Talbot's calculations show that the metabolism of the patient with obesity is in practically all cases a high normal metabolism and that of the patient showing malnutrition is below normal. Basal heat production is increased by epinephrine and is low in deficiency of the gonads except that it is not influenced by androgen.

While the cholesterol in the blood is usually found much elevated in myxedema and depressed in toxic goiter, the fact that the basal metabolism and the cholesterol level change independently of each other suggests that some factor other than the thyroid may influence the cholesterol level.

Tests for urinary hormones promise important and interesting information as they become refined, but much has yet to be learned about the physiologic effects of these substances before they become of routine usefulness in clinical practice.

Effective treatment of most of the various endocrine disorders awaits more accurate understanding of the underlying pathologic conditions as well as reliable

therapeutic instruments and procedures. This eminently sane review of the present status of endocrinology should be studied by all who are bewildered by the present day literature on the subject.

EUGENE H. SMITH, Ogden, Utah.

THE GONADOTROPIC ACTIVITY OF THE ANTERIOR PITUITARY GLAND IN RELATION TO INCREASED INTRACRANIAL PRESSURE. W. R. HENDERSON and I. W. ROWLANDS, Brit. M. J. **1**:1094 (May 21) 1938.

Although relatively brief, this article does not lend itself to abstracting; however, it is apparently shown that the gonadotropic activity of the pituitary varies with age, being small in amount in early childhood and increasing to the end of the period of sexual activity. In women there is a rise in activity at the menopause but in men a rise does not occur until the seventieth year. The article is not conclusive.

ROYSTER, University, Va.

DIABETES MELLITUS IN INFANCY. K. H. TALLERMAN, Proc. Roy. Soc. Med. **31**:764 (May) 1938.

An 18 month old boy was presented as being listless and drinking pints and pints of water. For the last two days he had been drowsy, with his breathing deep and heavy. The urine was loaded with sugar, and the blood contained 400 mg. per hundred cubic centimeters. The child was at once given 20 units of insulin and within an hour 30 Gm. of dextrose by mouth. Two hours later symptoms of hypoglycemia developed, and 170 cc. of 10 per cent dextrose solution in saline solution was given intravenously within the next four hours. The next day he was alert and bright.

WILLIAMSON, New Orleans.

THE THYMUS MYTH. T. G. WILSON, Irish J. M. Sc., March 1938, p. 113.

Wilson concludes that pathologic enlargement of the thymus is diagnosed far too often. He feels that all other causes of respiratory distress should be ruled out first and that direct inspection of the larynx should be made to rule out congenital laryngeal stridor. That thymic death occurs is a myth. The error results from mistaking the normal large thymus found in well nourished children for the pathologically enlarged gland noted in cases of sudden death.

SNELLING, Toronto, Canada.

DIABETES AND TUBERCULOSIS IN THE CHILD. P. NOBÉCOURT, P. DUCAS and SCHEINMANN, Arch. de méd. d. enf. **41**:425 (July) 1938.

Among adults, tuberculosis is frequently found as a complication of diabetes; as a matter of fact, with insulin therapy, it is one of the chief causes of death. Before the use of insulin, the short course of diabetes in children (averaging among American clinicians about two and one-half years) prevented evolution of coincident phthisis, but since that period it has been possible to observe the course of this complication in a number of young subjects. In a series of 519 cases of juvenile diabetes reported by White, there were 8 in which tuberculosis was also present; the authors observed only a single patient with this complication in a series of 20 patients with diabetes.

When a diabetic child becomes tuberculous, it is incumbent on the medical attendant to study (1) the influence of tuberculosis on the diabetes and (2) the influence of the diabetes on the tuberculosis.

With respect to the first observation, it is recognized that in the adult tuberculosis aggravates the disequilibrium of the glucosides, favors the onset of acidosis and establishes a relative resistance to insulin. In the child the effect is similar but much less marked. Like action may follow the invasion of other febrile diseases, such as the acute exanthems. A rigid dietetic regimen must be followed to prevent disaster.

The role of diabetes in the evolution of tuberculosis will depend on the therapy instituted. In 18 of 19 instances compiled from the literature diabetes preceded the appearance of tuberculosis by from one to eight years. The evolution of tuberculosis will be influenced by the character of the treatment for diabetes both before and after the onset of tuberculosis. In this connection, it should be borne in mind that in diabetic children tuberculosis has an acute onset.

AMESSE, Denver.

Diseases of the Muscles, Bones, Joints and Lymph Glands

APPARENT MYOPATHIC AMYOTROPHY IN TWO UNIVITELLINE FEMALE TWINS. ANDRÉ-THOMAS, PAISSEAU, SORREL and SORREL-DEJERINE, Rev. neurol. **67:** 567, 1937.

Two premature twins, identical in every respect, showed paralysis and amyatrophy of the neck, trunk and extremities, most marked in the supinator, triceps, brachialis and extensor muscles of the lower extremities. The proximal segments of the extremities were more involved than the distal. There were no disturbances of sensation, speech or intellect. According to the mother, the twins had developed normally until the age of 18 months, when the weakness began insidiously and progressed gradually. No similar condition could be found in other members of the family. The condition was not similar to polyneuritis, acute anterior poliomyelitis, Charcot-Marie disease or myatonia congenita. It had some resemblance to muscular atrophy of the Werdnig-Hoffmann type but differed from this condition in several respects. The affected muscles showed an increased threshold to electric stimulation but no reaction of degeneration. Fibrillations were absent, and muscle jerks were not obtained in response to mechanical stimulation. These features suggested that the condition was more akin to myopathy, although it did not conform to any of the known categories. Etiologically, no evidence of syphilis was found, and antisyphilitic treatment was without effect. The disease can hardly be called familial, since identical twins genetically represent one organism.

LIBER, New York. [ARCH. NEUROL. & PSYCHIAT.]

STILL'S DISEASE AND GLANDULAR LESIONS. S. LEVI, Riv. di clin. pediat. **36:**409 (May) 1938.

Still's disease in a girl of 11 years is described. The right epitrochlear gland was removed and studied histologically; it showed dilatation and obstruction of the lymphatic vessels and circumscribed foci of postinflammatory sclerosis.

HIGGINS, Boston.

CASES OF BORNHOLM-LIKE MYALGIA. W. THIELE, Deutsche med. Wchnschr. **64:**7 (Jan. 7) 1938.

In 1932 Sylvest described acute epidemic myalgia occurring unexpectedly among well subjects. First he called this symptom complex Bornholm disease because it occurred in Bornholm, Germany; later he changed the name to myalgitis acuta epidemica. The disease occurs in persons of all ages. It most commonly affects the muscles of the trunk, less frequently the muscles of the extremities. There is fever in the majority of instances. The condition is of short duration, and recovery is usually complete. The disease occurs most frequently in August and September. No special therapy is needed.

Thiele describes 5 cases in adults, which occurred in Rostock, Germany. He considers them instances of the disease described in Bornholm.

KERETZTURI, New York.

Skin Diseases; Allergy

CAUSATION AND TREATMENT OF DERMATITIS. R. HALLAM, Lancet **1**:1259 (June 4) 1938.

Recognizing the important roles which low grade physical and mental resistance may play in dermatitis, the author suggests the following simple classification of dermatitis: (1) traumatic dermatitis, (2) atopic dermatitis (infantile eczema and sequelae) and (3) sensitization dermatitis (often referred to as eczema).

Traumatic dermatitis is an inflammatory reaction of the skin following application of an external irritant. Primarily, traumatic dermatitis is limited to the area of skin which has been in contact with the particular irritant, whereas sensitization dermatitis tends to spread and involve even distant areas.

Eczema, often classified as a sensitization dermatitis, has not been satisfactorily explained. The multiplicity of the occasional causes suggests that it is a syndrome and not a morbid entity, the predisposition being the common factor.

Infantile eczema is now commonly regarded as an entity and distinguished from other eczemas. It is often referred to as atopic dermatitis. In a considerable proportion of cases, if not in all, it is a familial disposition.

The method of distinguishing between the various types of dermatitis depends in large measure on the taking of a thorough, discriminate history.

As far as treatment is concerned, elimination of the cause and rest and protection are applicable to all the patients.

In infantile dermatitis cleansing the skin with zinc oxide and kaolin lotion is advocated in place of soap and water. LANGMANN, New York.

THE NATURAL HISTORY OF STRAWBERRY NEVI. W. A. LISTER, Lancet **1**:1429 (June 25) 1938.

From a review of the literature and a study of a series of cases it appears that strawberry nevi of infants have a natural history entirely different from that of any other type. The essential point of distinction is that they enjoy a period of more or less rapid growth (never over a year) during the first few months after their appearance. Then retrogression sets in; and they disappear of their own accord, on the average about the fifth year of life.

It follows that drastic measures for the destruction of these nevi are inadvisable, and treatment should be expectant and conservative. LANGMANN, New York.

ANAPHYLACTIC SENSITIZATION. A. G. ALARCON, Rev. mex. de puericultura **8**:165 (March) 1938.

Alimentary sensitization is brought about by an upset in the digestive processes whereby the proper breaking-down of the proteins is incomplete. There is then an absorption of these abnormal substances, producing the allergic phenomena. Alarcon describes in detail the mechanics of the pylorus. He believes that the greater part of the foods producing anaphylactic sensibility are liquids rather than solids. HERRON, Monroe, La.

DISTRIBUTION OF PRINCIPAL TYPES OF ANGIOMA. A. TOURAINE, Bull. Soc. franç. de dermat. et syph. **44**:2054 (Dec.) 1937.

This study of 155 patients with 193 angiomas of diverse types may be summarized as follows: With the exception of the stellate angiomas, which occurred with equal frequency in males and females, 70 per cent of the angiomas occurred in females. Angioma is rarely familial and shows no definite predilection for the first born. In 75 per cent of the cases the lesion was single. Stellate angioma occurred most frequently on the face (nose and cheeks) and neck. Flat angioma

was located on the face and neck in 90 per cent of the cases. The most common locations for tuberous and cavernous angioma were the forehead, chest, cheeks and arms. Association with other congenital dysplasias was relatively rare. From an etiologic standpoint, heredity and traumatism seemed negligible factors. Twenty-five per cent of the patients had prenatal syphilis.

LAYMON, Minneapolis. [ARCH. DERMAT. & SYPH.]

ADENOMA SEBACEUM AND ITS ROLE IN A NEUROCUTANEOUS SYNDROME; TUBEROUS SCLEROSIS AND ITS RELATIONSHIP TO RECKLINGHAUSEN'S DISEASE. A. KVEIM, Acta dermat.-venereol. **18**:637 (Oct.) 1937.

Kveim describes 3 cases of adenoma sebaceum with the typical cutaneous lesions and involvement of the central nervous system (epilepsy and mental retardation). Tumors were demonstrated roentgenologically in the cerebrum and around the ventricles. In all cases there were changes in the retina and periostitic deposits in the small bones and in the skull. In all the cases there was a history indicating probable inheritance of the condition. The author believes that adenoma sebaceum is merely a symptom of tuberous sclerosis and that there is some genetic connection between these conditions and Recklinghausen's neurofibromatosis. All these conditions are, according to the author, caused by anomalies of fetal differentiation. He mentions the fact that the epidermis and the central nervous system are both formed from the ectoderm, and this explains the logical connection between the cutaneous lesion and the disturbances of the nervous system. In regard to the tumors, which consist of cells difficult to classify, the author thinks that these have developed through some embryoplasmatic dysplasia.

ASTRACHAN, New York. [ARCH. DERMAT. & SYPH.]

Miscellaneous

HUMAN ASCITIC FLUID AS A BLOOD SUBSTITUTE IN EXPERIMENTAL SECONDARY SHOCK. H. A. DAVIS and C. S. WHITE, Proc. Soc. Exper. Biol. & Med. **38**:462 (May) 1938.

Ascitic fluid was obtained from 3 persons suffering from portal cirrhosis and after cross matching was injected into the blood stream of 15 dogs in which shock had been produced by graded hemorrhages. It was found that the human ascitic fluid was capable of raising and maintaining the blood pressure in these animals suffering from secondary shock. The results indicate that human ascitic fluid is of value as a substitute for whole blood.

HANSEN, Minneapolis.

LEAD ANALYSES OF HAIR AS AN INDICATION OF EXPOSURE TO LEAD. J. L. MELNICK and G. R. COWGILL, Proc. Soc. Exper. Biol. & Med. **38**:899 (June) 1938.

Analyses of the hair of 30 human subjects indicate that the amount of lead found corresponds with the degree of exposure to this element. The lead in the hair could not be washed out. That lead is not "excreted" through the hair is shown by experiments in which lead salts were fed to young white rats: No increase in the lead content of hair was found.

HANSEN, Minneapolis.

VALUE OF CRÈCHES. J. FREIRE DE VASCONCELOS, Arch. de pediat., Rio de Janeiro **10**:395 (May) 1938.

The author pleads for more scientific standardized care of infants.

SANFORD, Chicago.

EARLY OBSTETRICS AND PEDIATRICS IN BRAZIL. A. BEZERRA, Bol. d. Inst. de puericultura, Rio de Janeiro **1**:95, 1938.

Bezerra quotes a chapter from the book "De Medicina Brasiliensi," by William Pies, published in 1648. A white man and a Negress were the parents of twins, delivered by Pies. One child was perfectly white, with light hair, and the other was black, with greenish eyes and black crinkly hair. SANFORD, Chicago.

OXYGEN THERAPY IN CHILDHOOD. J. H. P. JONXIS, Nederl. tijdschr. v. geneesk. **82**:2675 (May 28) 1938.

Jonxis stresses the importance of oxygen therapy. The indications for it and its effects can be judged best by determining the oxygen saturation of the arterial blood. Cyanosis is not always an indication for giving oxygen. The causes and consequences of hypoxemia are reviewed. The different ways of administering oxygen are discussed, and a new model oxygen tent, representing an improvement of an already existing one, is described.

VAN CREVELD, Amsterdam, Netherlands.

Society Transactions

CHICAGO PEDIATRIC SOCIETY AND CHICAGO MEDICAL SOCIETY

JOSEPH K. CALVIN, M.D., *President*

Joint Meeting, Jan. 11, 1939

GEORGE F. MUNNS, M.D., *Secretary*

GYNECOLOGIC PROBLEMS OF THE ADOLESCENT GIRL. DR. EDWARD ALLEN.

Adolescence has been defined as the period of life between puberty and maturity. This must be taken as an average; puberty or maturity may occur at varying ages, and each is an indefinite state. Some disturbances of pelvic anatomy and physiology are based on lack of development, many times dating back to childhood. This is particularly true of marked glandular dyscrasias, such as hypothyroidism, obesity and pituitary disorders. When parents are intelligently guided in the medicinal and psychic problems of their daughters' reproductive systems, many of the gynecologic problems of adolescence and later life may be avoided, for example, primary dysmenorrhea, amenorrhea, metrorrhagia, infantilism of the reproductive organs, including the breasts, vaginitis and its atresias, frigidity and vaginismus.

Careful routine examination of the pelvis of the growing girl is even more important than routine care of the teeth. In many cases absence of the vagina has been unrecognized until after marriage. The imperforate hymen is common; it usually is not recognized until the retention of menstrual blood produces symptoms or a tumor large enough to attract attention. Most gross abnormalities in the adolescent genital tract may at least be suspected by means of careful inspection combined with rectal examination. The hymenal orifice in the vast majority of girls is sufficiently large to permit, without undue pain, necessary digital or instrumental examinations.

Maldevelopments of lesser degree, such as infantile uterus or congenital retroversion, are important factors in the production of primary dysmenorrhea; when the condition is not so caused, it is probably due to glandular imbalance. In most cases, dysmenorrhea can be relieved by heat, rest and simple analgesias; when these measures are insufficient, treatment with endocrine substances should be advised. These are powerful medicines with many side effects as yet unknown, and their indiscriminate use for growing girls is not advised.

The first year of menstrual life is usually characterized by marked irregularities similar to those seen at the other end of the menstrual cycle, the menopause. There may be long periods of amenorrhea; one should consider the possibility of pregnancy if amenorrhea is long continued. Menorrhagia may be disregarded unless it is greatly prolonged or profuse enough to change the blood picture. Metrorrhagia demands prompt and thorough examination; there is no age limit for malignant growths.

Precocious menstruation should be extensively investigated. It is usually caused by tumors of the sexual glands, the adrenal cortex or the pineal body. Prolonged serious bleeding may require the combined knowledge of an endocrinologist, a hematologist, a pathologist and a gynecologic surgeon.

Thyroid therapy apparently offers the greatest possibility of glandular cures; even when the basal metabolic rate is normal or slightly increased it should be given a trial. The estrogenic and pituitary preparations have been found less effective than some investigators have reported. Simple dilation and curettement,

sometimes frequently repeated, may ultimately bring about cure and will serve at least as an emergency measure to control bleeding and to allow the patient to regain a measure of strength. Multiple blood transfusions are often necessary and in a few instances are adequate therapy.

Pelvic infections, especially tuberculous, must always be considered. Local signs such as a low grade fever, loss of weight, fatigue and pulmonary or gastrointestinal symptoms call for careful roentgen examination of the chest and abdomen.

The use of either roentgen or radium therapy in an attempt to produce temporary amenorrhea in cases of adolescent bleeding is not advised. Complete and permanent castration occurs in from 30 to 50 per cent of the cases. When conservative methods have failed and life is threatened, vaginal hysterectomy should be considered rather than castration by irradiation.

Vaginitis is not found so frequently in the adolescent as in the pubertal, adult or postmenopausal period. The vaginal mucous membrane is at its highest point of resistance, and the vagina is not subject to infection by the usual methods. The psychic effect of discharge and irritation at this impressionable age is pronounced, however, and it must be emphasized that an intact hymen should not interfere with diagnosis or treatment; in fact, inadequate drainage may be the sole cause. Trichomonas vaginitis, yeast infections and gonorrhea usually respond to appropriate treatment if there is no focus of reinfection. Congenital erosions of the cervix are probably the commonest cause of discharge; they can usually be taken care of by superficial cauterization of the eroded area with the nasal cautery loop.

In conclusion, I urge those engaged in the practice of pediatrics and obstetrics to instruct the mothers of growing girls consistently and patiently in an intelligent understanding of the far-reaching effects of the psychic and anatomic functions of their daughters' sexual organs. The intact hymen is neither a necessity for nor a criterion of virginity. Developmental abnormalities or fixed psychic difficulties can be prevented much more simply than they can be cured. A concerted effort by the medical profession for education along these lines would do much toward the happiness of this generation of mothers, and they in turn would pass it on to their daughters, with gratifying results.

BEHAVIOR PROBLEMS OF ADOLESCENTS. DR. PAUL L. SCHROEDER.

Adolescence is an age of tremendous change in all phases of its development. While the constitutional changes of puberty are fairly well understood, there is much to be learned about the emotional stress and strain of adolescent years.

This study is concerned with the function of the adolescent as a thinking, feeling person reacting as a whole being to stimuli from without and within; it deals with the one who has behavior difficulties rather than with so-called normal adolescents. Fifty-one cases are used as a basis for discussion. The findings offered are tentative and will be checked later by a more comprehensive study on a larger group.

The ages of the children ranged from 13 to 18 years. They were about equally divided as to sex; 6 were Negroes and the remainder were white. They came, in the main, from families of average size, half of which had three or more siblings. The largest family had twelve children, the youngest of whom was the child in trouble. It was noted that the largest number of children were the second born; the next largest, the third born. The first child appeared as a problem in 20 per cent of cases; only 10 per cent of the group were youngest siblings. Five of the children were reported to be "only" children, but 3 of these lived in foster homes.

Half of the group were referred by the Juvenile Court. The next largest group came at the request of parents, social agencies and child care organizations. Teachers, doctors and clergymen referred the remainder. The reasons for examination varied, the most common being unsatisfactory school work. Truancy, sexual delinquency and stealing were next. Sexual delinquency was as common

as truancy among girls; no girls were referred for stealing. Sexual delinquency was only half as frequent among boys as among girls. Incorrigibility, with violent behavior such as disobedience, quarrelsomeness, assault, temper and arson, ranked highest in all behavior problems. Less frequent causes of referral included attempted suicide, pregnancy, enuresis, nervousness, hysteria, epilepsy, masturbation, robbery with a toy gun and inability to talk.

It has repeatedly been observed that a large proportion of these juvenile delinquents come from broken homes; this was true of half of this group. Only one third of the group attended high school; 4 were defective mentally and were being taught in special rooms; 7 had dropped out of school; 2 attended trade school, and 1 was in a school for the deaf.

The general health of this group of children was fairly good. Six of the boys showed some developmental or nutritional disturbance. Half of the girls showed vaginal evidence of sexual activity. Three girls had visual defects. Thirteen children had intelligence quotients under 70. Only 2 had superior intelligence.

The most common psychiatric diagnosis was feeblemindedness, in 1 instance combined with psychosis. Next most common were adolescent rebellion and emotional dependence, each occurring in 4 cases. Other diagnoses were inadequate personality, conflict over adoption, reaction depression, feelings of incestuous guilt, epilepsy, homosexuality, schizophrenia, hysteria, parental rejection and psychopathic personality. In 1 instance it was felt that a behavior difficulty did not exist and in another that there was parental overanxiety.

In summary, I wish to call attention to the great variety in kind and severity of behavior problems. No single cause has as yet been found, and each case presents an individual problem. In the period of adolescence there is a tremendous drive for self expression. Parental resistance to the child's growth is deeply involved. Family relationships must be reoriented to permit breaking of the infantile emotional connection with the parents. Adequate early training will assure a more comfortable adolescence. There is apparently a direct relation between the violence of the reaction of the adolescent and the resistance by his parents to his emergence into adulthood.

ENDOCRINE DISORDERS IN ADOLESCENCE. DR. ELMER L. SEVRINGHAUS (by invitation), Madison, Wis.

Disorders of growth include both dwarfism and gigantism. Dwarfism may be associated with obesity and retardation in the adolescent development or with other features, such as diabetes, or may occur by itself. It is important to attempt to identify the cause in order that etiologic treatment may be supplied. If, however, the epiphyses are still open, an anterior pituitary extract containing the growth hormone may be administered no matter what the cause, being continued so long as growth response occurs or until the epiphyses are shown by roentgen study to be closed. Gigantism is difficult to diagnose until it is too late for treatment. What may be done to limit the growth is still uncertain.

Disturbances of sexual maturity may include infantilism, which is associated with obesity in Fröhlich's syndrome, may be associated with underweight, as with the curious asthenic types, may appear in the eunuchoid form or may appear in the masked form evident chiefly by menorrhagia and irregular menstruation. Again, the disturbance may appear as precocious adolescent development. When the infantilism is associated with obesity, that feature must be treated by limitation of diet. Thyroid therapy is occasionally helpful if the basal metabolic rate is low. For all these manifestations of underactive gonads it is now possible to use hypodermic injections of an anterior pituitary extract containing the gonadotropic factor to stimulate response. Results are variable, depending on the capacity for response of the gonads. Treatment of boys should be continuous, and that of girls should be interrupted and cyclic, since the ovaries operate in cycles. Precocious adolescence may be associated with pituitary, pineal, thymic, adrenal or ovarian disturbances, and it is important to identify the organ etio-

logically involved. Often this cannot be done, and all that is possible is rather watchful psychologic care, with search for evidences of tumor and an attempt to promote bony growth before the epiphyses unite and stop further gain in height.

Thyroid disturbances include cretinism, which is easily diagnosed and known well, and thyrotoxicosis, which is relatively uncommon in adolescence. Conservative treatment for the latter is advised. Iodine salt for the prevention of goiter should be used universally in the entire goiter area. There is no danger from it unless the salt intake is so small that the iodine supply is inadequate.

Parathyroid disturbances are uncommon, but either tetany or hyperparathyroidism is important. The treatment of tetany involves a low phosphorus diet with high intake of calcium by medication and often the oral use of dihydrotachysterol. Hyperparathyroidism calls for diagnosis and surgical treatment before there has been significant damage to the kidneys as well as to the bones.

Disorders of the adrenals, such as Addison's disease, are rare in adolescents.

Pancreatic disturbances include diabetes and hypoglycemia. Diabetes in childhood is characterized especially by instability and by cycles of tolerance; the important features of treatment are giving the child a diet adequate for growth and keeping him as nearly as possible free from glycosuria at all times. Hypoglycemia may be the cause for uncommon attacks of hunger leading to obesity. This calls for special types of diet. Obesity may also be associated with a familial history of the condition, otrhopedic disturbance or lack of exercise, or it may follow encephalitis. In all cases dietary restriction is necessary.

DISCUSSION

DR. A. H. PARMELEE: It is obvious that the fundamental science of the endocrine system, from the point of view of the gynecologists or of the man who is particularly interested in behavior problems, is well taken care of. However, some things need to be considered from the standpoint of what we, as general practitioners and as pediatricians, have to do with the adolescent child. Mothers and parents in general are actually confused by adolescence. As one mother expressed it to me, "My older girl, now in high school, says I am experimenting on her so that I will be ready to take care of her younger sister."

Our function, it seems to me, is to try to direct parents in this rather difficult stage of their children's growing up and becoming mature. It seems important to see that they do not alienate their children. As I come in contact with adolescent children, I find that the one mistake parents make continually is not to give the children credit for the intelligence they have. Actually, from the standpoint of intelligence, the high school child, the adolescent child, is perfectly capable of holding his own with his parents. The difference lies almost exclusively in the element of experience. The parents' superiority is purely a matter of intellect plus judgment that has come from experience. Therefore, the parents' function, after the child reaches the age of puberty, is that of a vitally interested spectator, watching to see the result of the previous training, standing ready to give advice when asked but not inflicting it when it is not sought. With that sort of attitude, the parents allowing the child to feel that they are considering him an intelligent person and talking to him on the same level, an adolescent boy or girl will come to them for advice, and early training will adequately express itself and bear fruit in due time. Many of the problems encountered are similar to the problems of the climacteric, which is simply adolescence in reversal.

In stable health the glands of internal secretion are more or less in a state of equilibrium, but when the sudden growth of puberty occurs they are not. There is an imbalance. This is manifested by instability of the vasomotor system, flushing, blanching, sudden fainting spells and peculiarities of circulation and of the action of the heart. Every autumn half a dozen children are brought to me from high school, having been told that something is wrong with their hearts. I nearly always find definite tachycardia and possibly a murmur, which

are characteristic of puberty and should in no way interfere with normal activity. Recently pediatricians have taken over the field of adolescence, I think rightfully, because it has been neglected and because pediatrics should include the care of the human organism during the period when growth and development are dominant factors.

DR. BERT I. BEVERLY: I should like to emphasize a few of the points that were made.

Adolescence is a period of growth and development. As such, it brings up the general problems of growth and conditions peculiar to this age. During adolescence, the young child rapidly "grows up" and tries to make an adjustment to society on an adult basis. Many problems arise in his mind, the solution of which is essential to his successful growing up. The seriousness of these problems is determined to a large extent by the methods which have been used in rearing the child from birth.

Since adolescence is characterized by marked exaggeration of sexual impulses and the development of sexual attraction, the first problem has to do with sexual adjustment. The child who has been convinced that everything connected with sex is wicked and wrong will have a much more difficult time than one who has been intelligently instructed. The second problem has to do with independence. The adolescent feels grown up but will still accept help if his independence is granted. The third problem has to do with heterosexual adjustment. The fourth has to do with feelings of inferiority and the numerous fears and experiences peculiar to each individual.

Just one word about treatment. The failure of the use of force and the reform school is well known. The only logical treatment is to gain the confidence of the maladjusted adolescent and to help him in the solution of his problems.

DR. JAMES H. HUTTON: The remarks of Dr. Parmelee and Dr. Beverly make me wonder if the story that came from Hollywood was much overdrawn. A young star was aked to fill out a questionnaire. One question was, "At what age should parents be taken into your confidence?" Her reply was, "As soon as the parents can take it."

I add my plea to that of Dr. Allen that these disorders be recognized early and treated adequately with the idea of preventing more serious disorders in later life. This, it seems to me, is one phase of preventive medicine. The best time to treat an endocrine disorder is when it is recognized. True, the child may sometimes "outgrow" it, but what he most often outgrows is his opportunity for permanent relief.

It is gratifying that neither of the essayists mentioned the determination of the amount of hormones in the blood or urine as a requisite to diagnosis or treatment. It was demonstrated by Frank that while these determinations are interesting they do not necessarily indicate the source of the trouble, while Burch and his co-workers showed that the endocrine status of the patient cannot be determined by examination of the endometrium. It is likely that eventually a diagnosis will be made in most cases from the history, physical examination and a few simple laboratory procedures.

The basal metabolic rate unfortunately does not indicate how much thyroid the patient needs. Indeed, the rate may be low when the thyroid gland is not primarily at fault and the patient cannot be benefited by the administration of thyroid. On the other hand, in the presence of combined thyroid and pituitary deficiency the rate occasionally may be well above normal and the pulse rapid. In such cases the basal metabolic rate and the pulse return to normal under adequate thyroid medication.

Dr. Sevringhaus is right in urging that the dose of thyroid be increased slowly. However, in private practice, when one can watch the patient carefully, the dose may be increased more rapidly than he has indicated. While frequent determination of the basal metabolic rate is desirable, one can control the dose well by careful clinical observation.

The frequency with which physicians are confronted by endocrinopathies is not sufficiently appreciated. Yesterday a public health officer came to my office complaining of the number of endocrine defects he had encountered while supervising the examination of high school students. These defects were indicated by obesity, deficiencies in growth and hypoplastic genitalia. He felt, as I do, that they should have been recognized and properly treated before the victims reached high school.

One can more easily and adequately treat hypofunctional disorders than the counterpoised hyperfunctional conditions. Fortunately, hypofunction is the more common type of disorder.

I differ with Dr. Sevringhaus as to the handling of candidates for gigantism. By using roentgen doses smaller than the gynecologists use as so-called stimulating doses one can frequently retard the rate of growth and perhaps hasten closure of the epiphysial lines. At any rate, that seems to have happened in a number of cases I have had under observation for several years. It is hardly necessary to add that my associates and I have not used massive doses, which would destroy or impair pituitary function. Until the roentgenologists become more certain of the biologic effects of small doses of roentgen rays, one may assume that, as clinical observation suggests, they have a regulatory rather than a stimulating effect.

The belief is current that in victims of parathyroid tetany there develops a tolerance for parathyroid substance, so that eventually very large doses are necessary to control the symptoms. It is also said that vitamin D or a chemical fraction of it (dihydrotachysterol) will control the symptoms. But I have had under observation for eleven years a woman whose tetany began after partial thyroidectomy, in whose case this is not true. Vitamin D and dihydrotachysterol are ineffective, but the same amounts of solution of parathyroid are effective now as they were at the onset.

DR. WILLIAM BROWNE: Most of the disorders that gynecologists encounter in adolescents are disturbances of menstruation or developmental defects, and up to the present time disorders of menstruation have been treated rather indiscriminately with a gonadotropic substance from the urine of pregnant women. They do not respond as the menorrhagia of maturity does. The amenorrheas of adolescence are hard to detect, because it is hard to say when a given girl should begin to menstruate.

On the other hand, if a girl lags in development it may have a definite psychic effect, and in case of a girl who lags behind her group in physical and in psychic development it may be well to substitute, at the age of 17 or so, administration of estrogenic preparations, which if used extensively enough will produce some change, particularly in secondary sexual characteristics. At the present time one can give much more estrogenic substance than was possible ten years ago. The total amount can be large.

Of the developmental defects, the most startling are total absence of the vagina and imperforate hymen. Girls with these conditions certainly deserve an early diagnosis. I received a letter from a woman whose condition was not diagnosed until she was 26; there was complete absence of the vagina, and it was doubtful if she had a uterus. She had contemplated marriage but knew it could not be consummated. An imperforate hymen had caused trouble before it was recognized. These conditions are simple to handle, although there are certain difficulties. It is not enough to make an incision and let the accumulated menstrual blood run out. A a weak solution of formaldehyde may be injected to mix with the blood before it is drained out, and the incision should be packed with antiseptic gauze to avoid infection.

DR. W. C. DANFORTH: There are a number of problems concerning the adolescent girl which come frequently to the attention of the gynecologist. In many instances he can best serve her interests by assuring an anxious mother that nothing serious is wrong and that the girl should not be subjected to treatment. Irregularities of menstruation, common enough during the years immedi-

ately following maturity, call for no treatment unless there is something besides the mere failure to follow a regular periodicity. In a considerable group of cases hypothyroidism is found. In these cases the administration of thyroid is of value. Some of these girls are overweight, tire easily and fail to accomplish their school tasks easily. They may often benefit greatly from thyroid medication. I do not believe it is either wise or useful to treat them by injections of one or another glandular preparation. Such treatment is not beneficial; it subjects the family to needless expense and fixes the mind of the adolescent girl to an undesirable degree on her usually unimportant deviation from the average normal status. Severe bleeding at the time of maturity or soon after may become a real problem. Fortunately, time works on the side of the physician in these cases, and in most of the patients the condition ultimately regulates itself. For the minority, who bleed enough to necessitate attention, management should be as simple as possible. Rest, including withdrawal from school or social activity, may help greatly. A young college student who bled excessively recovered promptly when sent home to the quiet community from which she came. Recurrence followed her return to college, and relief was again obtained when she returned home. Glandular treatment in these cases sometimes helps but should not supplant reduction of activity. In my experience curettage is seldom needed. Irradiation should be restricted to the rare patient whose condition has resisted all conservative treatment and whose bleeding has become dangerous. It is sometimes necessary to impress on the family of the patient that preservation of health in general, and of the health of the reproductive system in particular, is of greater importance than the maintenance of any form of activity, even the pursuit of a prescribed course of education.

Leukorrhea in the young girl is sometimes a problem. As little local manipulation as possible should be used. If the discharge is sufficient in quantity to render treatment desirable, the cautery should be conservatively used in cases in which there is endocervicitis with an area of erosion about the external os. Usually four stripes, placed equidistant from one another, are sufficient. Douches are not favored. In cases of trichomonas infection the usual effective form of antiseptic may be used. It may be necessary to open a rather tightly closed hymen to permit drainage and to permit access to the vaginal tract for treatment. If there is no more than slight moisture, the girl may be dismissed without any treatment

In the management of primary dysmenorrhea the simplest possible treatment is best. Dilation and the insertion of stems and tubes in the cervix should be performed only after all the more conservative resources have been tried. A capsule containing ephedrine and amytal often helps, and it appears harmless. Present day studies in the physiology of the reproductive tract may in time provide simpler, more effective and less expensive remedies than those now available. In some cases glandular therapy is satisfactory.

In general, from the standpoint of the gynecologist, the disorders of adolescence in the girl should be managed in the simplest manner. Her attention should be directed toward her pelvic organs as little as possible. In the great majority of cases in my experience radical therapy or treatment requiring repeated local manipulation has not been necessary.

Dr. George Mohr: Comment to the effect that pediatricians now particularly interest themselves in the adolescent period is appropriate. I should like to emphasize the fact that the problems of adolescence really are met and dealt with long before the age of adolescence is reached. The adolescent period is in effect a repetition of the period between the ages of about 3 and 5 or 6 years, during which the child steps from the position of a nursling to that of a school child, who must deal with a more complicated environment and more responsibilities. The general manner in which he solves the problems of this period of life largely determines the efficiency of his efforts in meeting the problems of adolescence. A wise handling of this early period of life constitutes the best prevention for disturbances during the adolescent period.

I wish to emphasize that adolescence is often an anxious period, both for the child and for the parents. To be sure, the nonanxious adolescent may get into difficulties. Dr. Schroeder has revealed some of the delinquencies that may be encountered. But almost as many adolescents encounter difficulties by virtue of the anxiety they feel in stepping into the responsibilities of adult life. These anxieties require the sympathetic understanding of parents and pediatricians.

I should like to say one word for the parents. I think that they need as much help as the adolescents. A couple of weeks ago, I saw a terribly disturbed mother of an adolescent boy. The boy was rebellious and went his own way, and this conscientious mother centered her worry about the fact that he had no respect for her. She considered herself much remiss in rearing a boy who showed no respect for his elders. She needed a better understanding of this feeling and of meeting the problem; her problem became a different one when she followed the advice given by Dr. Parmelee, which was to accept the boy's efforts to go his own way and not to regard them as showing weakness on his part or on hers. I think that if parents are supported during this time, the whole period becomes less a problem and more a season of relatively normal and less questionable development.

I have my own reaction about this matter of adolescence. Judging from everything we have heard, I think that we ought to go home and be frightened and look after our adolescent children and our grandchildren, lest something be wrong with them.

Strange to say, nobody has said a word about normal adolescent children. There must be some like that.

Are we not perhaps overestimating, overglorifying or even exaggerating that fearful period? Were we not adolescents at one time ourselves? We may remember with some slight remorse or with a suppressed laugh some of the foolish things or the absurdities that we perpetrated at that period. This age of flaming youth we recall as the most joyous time of all, when we saw visions and dreamed dreams. After all, we survived this period, and I think there is hope that others now in the same position will overcome this bogey as we did.

Every period of life has its problems, its characteristics and perhaps its peculiarities. The newborn infant is lucky if he is born alive and stays well during his tender years. Middle childhood, adolescence and maturity all have their physical and mental risks. Even senescence has its hazards. So why worry so terribly about the adolescent period? It may chance to be a normal and happy time of life.

I am not a rebel, but I feel we should calm down, lest we go home and tell our children and grandchildren and the parents of our adolescent patients in grave and terrible alarm, "Beware, my children. You are now approaching a fearful ordeal. The period of adolescence is upon you." Should we do this? God forfend!

DR. ELMER L. SEVRINGHAUS: Some specific questions were brought up for discussion. One was why endocrine therapy with gonadotropic substance from the urine of pregnant women has been more helpful against menorrhagia near the climacteric than in adolescence. It has one specific action in the nonpregnant human female; it has a destructive action on the follicles, which can more easily be destroyed at the age of 40 than in the teens. Therefore I have advocated not using the concentrated urine for nonpregnant human females.

I think that the use of estrogen to stimulate retarded development and thus effect psychic adjustment in a girl of 17 is poorly advised, although it is common. Whenever large doses of estrogen are used the pituitary, already inhibited, is further retarded. One should not try substitution therapy at a period when one is trying to bring about full maturity. Dr. Hutton referred to roentgen therapy, suggesting that these patients will have hypopituitarism and that they should be under treatment early. I have friends who are tall and have no hypopituitarism, who have grown beyond the average stature and yet are not classed as pituitary giants. For mild deviations from the normal I object to roentgen therapy, which I understand is destructive and should not be applied to growing persons.

Book Reviews

Physical Diagnosis. By Richard C. Cabot, M.D., and F. Dennette Adams, M.D. Twelfth edition. Price, $5. Pp. 846, with 390 illustrations. Baltimore: Williams & Wilkins Company, 1938.

This well known text has been entirely revised and rewritten. With the collaboration of a junior author, Dr. Cabot has departed from his previous policy of discussing only the methods with which he has had personal experience. The present edition has been elaborated with the help of many members of the staff of the Massachusetts General Hospital and is to a considerable extent the work of a group. With the original arrangement as a basis, new chapters and sections and a great deal of new material has been added, the number of pages having been increased by 50 per cent. The illustrations, mostly new, are numerous and well chosen; they are clearer because of the glossier paper used in this edition.

Among the chief innovations is a well written chapter on taking the history.

This book now contains one of the most inclusive discussions of physical diagnosis in English. Yet it is clear and concise. The physical findings of infancy and childhood are more thoroughly covered than in most general texts on this subject.

This edition should help maintain the high position that Cabot's "Physical Diagnosis" has always held.

How to Conquer Constipation. By J. F. Montague, M.D. Price, $1.50. Pp. 244. Philadelphia: J. B. Lippincott Company, 1938.

This book is written primarily for the layman, but many physicians may find it of value. It emphasizes facts which, though known to the medical profession, are often given insufficient consideration. It is simply and humorously written, and the reader is made to understand why cathartics and patent medicines are harmful, what principles should underlie his selection of food and drink and why he should consult a competent physician if constipation is present.

You Can Sleep. By Edmund Jacobson, M.D. Price, $2.00. Pp. 269, with 40 illustrations. New York: Whittlesey House, 1938.

In this volume the author applies his previously described method of relaxation to sleep. The first half of the book describes the steps of progressive relaxation which are essential to sleep. There is a chapter on the sleep of children, pointing out the harmful effect of frightening radio programs and stories. In another chapter the author tries to prove that distressing dreams are due to lack of relaxation and advises against analysis of dreams. Other chapters are devoted to the thesis that worrying and distress at night can be dismissed in favor of relaxation if the patient desires it. The book includes a description of the laboratory methods of studying sleep.

The book is written for laymen. It is written mostly in conversational form and is easily understandable. It is critical of physicians and psychiatry. The author refuses to agree with those who consider relaxation largely suggestion.

Classic Descriptions of Disease. By Ralph H. Major, M.D. Second edition. Price, $5.50. Pp. 727, with 137 illustrations. Baltimore: Charles C. Thomas, Publisher, 1939.

This book is excellently commentated, well printed and well illustrated. It is the second edition of a valuable book on medical history. From a pediatric standpoint one could wish that more attention had been given to some pediatric conditions. Few are mentioned as such. However, the book is complete from the standpoint of internal medicine and is well written. In many instances translations from various languages of the original description of the disease are given.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
Place: Boston. Time: Sept. 3-5, 1940.

American Committee:
Chairman: Dr. Henry F. Hemholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.

Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St., W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

British Paediatric Association

President: Dr. Hector C. Cameron, 23 Devonshire Pl., Upper Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Sociedad Cubana de Pediatría

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

Société de Pédiatrie de Paris

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. Edward Clay Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: Hotel Chase, St. Louis. Time: May 15-19, 1939.

American Academy of Pediatrics

President: Dr. H. F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Netherland Plaza Hotel, Cincinnati. Time: Nov. 16-18, 1939.
Region I. Place: Waldorf-Astoria Hotel, New York. Time: June 1-3, 1939.
Region II. Meeting cancelled.
Region IV. Place: Hotel Leamington, Oakland, Calif. Time: April 6-8, 1939.

American Hospital Association, Children's Hospital Section

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

American Pediatric Society

President: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: Skytop Lodge, Skytop, Pa. Time: April 27-29, 1939.

Canadian Society for the Study of Diseases of Children

President: Dr. R. R. MacGregor, 142 Wellington St., Kingston, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. L. Emmett Holt Jr., Johns Hopkins Hospital, Baltimore.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.
Place: Skytop Lodge, Skytop, Pa. Time: April 26-27, 1939.

SECTIONAL

North Pacific Pediatric Society

President: Dr. Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Charles E. Conrad, 209-210 Professional Bldg., Harrisburg, Va.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Hyman Green, 483 Beacon St., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. John Schoonover, Republic Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Stewart H. Welch, 1117 S. 20th St., Birmingham.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.
Place: Montgomery. Time: April 17, 1939.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. G. D. Murphy, 112 Peach St., El Dorado.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.
Place: Hot Springs. Time: January 1939.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Harold K. Faber, 2341 Clay St., San Francisco.
Secretary: Dr. Hartzel H. Ray, 23–2d Ave., San Mateo.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Gilbert S. Osincup, 300 E. Colonial Dr., Orlando.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Coral Gables.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Charles Hall Farmer, 553 Walnut St., Macon.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.
Scientific Meeting—Place: Augusta. Time: Jan. 12, 1939.
Business Meeting—Place: Atlanta. Time: April 1939.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. C. V. Calvin, 144 Golden Hill St., Bridgeport.
Secretary: Dr. E. T. Wakeman, 129 Whitney Ave., New Haven.
Time: Three meetings a year.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. O. N. Torian, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

Louisiana State Pediatric Society

President: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.
Secretary-Treasurer: Dr. Philip C. de Verges, 312 Audubon Bldg., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester.
Secretary: Dr. Leslie O. Ashton, 842 Park Ave., New York.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.
Secretary: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Allan L. Richardson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. Ward L. Chadwick, 524 Medical Arts Bldg., Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. W. Myers Hunter, 306 N. Tryon St., Charlotte.
Secretary: Dr. J. R. Adams, 412 N. Church St., Charlotte.

Oklahoma State Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

South Carolina Pediatric Society

President: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.
Secretary-Treasurer: Dr. William Weston Jr., 1428 Lady St., Columbia.

Tennessee State Pediatric Society

President: Dr. William E. Van Order, 546 McCallie Ave., Chattanooga.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Jackson. Time: April 11, 1939.

Texas Pediatric Society

President: Dr. F. O. Calaway, 3306 Fannin St., Houston.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Houston. Time: May 9, 1939.

Virginia Pediatric Society

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. J. L. Blanton, 207 Fairmont Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, 450 Center Ave., Weston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. N. C. Wetzel, 2103 Adelbert Rd., Cleveland.
Secretary: Dr. Fred Rittenger, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

Bronx Pediatric Society

President: Dr. Samuel T. Levethan, 254 E. 184th St., Grand Concourse, New York.
Secretary: Dr. David Greene, 910 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Benjamin Kramer, 6 Pierrepont St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. Joseph K. Calvin, 2376 E. 71st St., Chicago.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. Harold Nesbit, 1719 Pacific Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. William O'Donnell, 1553 Woodward Ave., Detroit.
Secretary: Dr. Robert Mason, 5140–2d Blvd., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. L. H. Goldsmith, 384 Peachtree St., N. E., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. James H. Park Jr., 3717 Main St., Houston, Texas.
Secretary-Treasurer: Dr. Thomas J. Donovan, 2418 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Urban Busiek, 200 E. Pershing St., Springfield, Mo.
Secretary: Dr. Fred Speer, 2700 Parallel Ave., Kansas City, Kan.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. H. R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Paul M. Hamilton, 248 E. Main St., Alhambra, Calif.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Sidney D. Kramer, 61 Eastern Parkway, Brooklyn.
Secretary: Dr. Benjamin Stoloff, 1149 Eastern Parkway, Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. James Dobbins, 42-04 Ditmars Blvd., Long Island City, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry H. Donnally, 1612 I St., N. W., Washington, D. C.
Secretary-Treasurer: Dr. Harry A. Spigel, 2647 Connecticut Ave., N. W., Washington, D. C.
Place: Medical Society Bldg., 1718 M St., N. W. Time: 8 p. m., fourth Thursday of October, January, February, March and April.

Memphis Pediatric Society

President: Dr. Barton Etter, 376 S. Bellevue St., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Secretary-Treasurer: Dr. Samuel E. Kohn, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Secretary: Dr. Lucy Porter Sutton, 168 E. 74th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Robert Rosenthal, 437 Lowry Medical Arts Bldg., St. Paul.
Secretary-Treasurer: Dr. R. E. Nutting, 205 W. 2d St., Duluth, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Every month, except June, July and August.

Philadelphia Pediatric Society

President: Dr. Samuel Goldberg, 4546 N. Broad St., Philadelphia.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. T. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., first Thursday of each month, except July, August and September.

Rochester Pediatric Society

President: Dr. J. Merrel Parker, 11 N. Goodman St., Rochester, N. Y.
Secretary: Dr. H. C. Soule, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

St. Louis Pediatric Society

President: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: Third Friday of each month from September to June.

Seattle Pediatric Society

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Clement Smith, 1101 Beacon St., Brookline, Mass.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: Horace H. Rackham Graduate School, Ann Arbor, Mich. Time: Nov. 11-12, 1938.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Norman Survis, 650 Main St., New Rochelle.
Secretary-Treasurer: Dr. Elvira Ostlund, 131 Purchase St., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.